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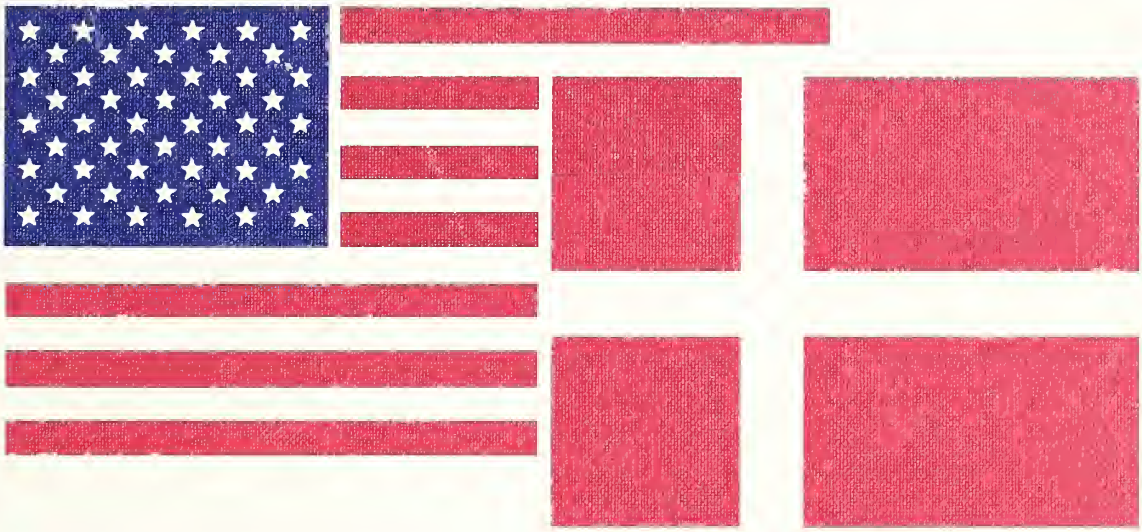
Multiple Primary Cancers in Connecticut and Denmark



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Multiple Primary Cancers in Connecticut and Denmark

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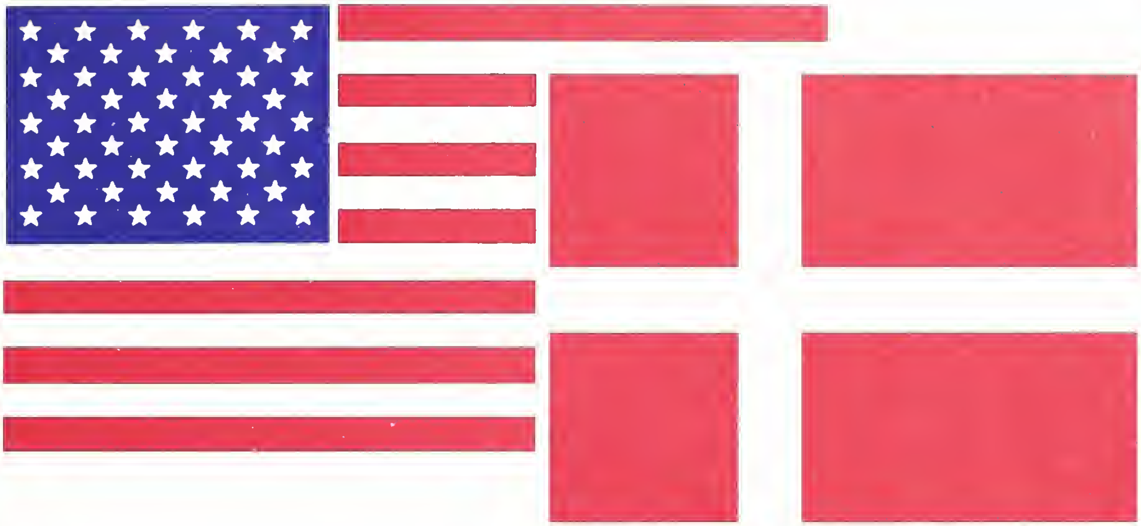
Multiple Primary Cancers in Connecticut and Denmark



National Cancer Institute

Danish Cancer Registry

John D. Boice, Jr.
Rochelle E. Curtis
Ruth A. Kleinerman

Hans H. Storm
Ole M. Jensen
Hjalgrim S. Jensen

John T. Flannery
Joseph F. Fraumeni, Jr.

Connecticut Tumor Registry

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I. Introduction

Introduction to the Study of Multiple Primary Cancers [1]

John D. Boice, Jr.,[2] Hans H. Storm,[3] Rochelle E. Curtis,[2] Ole M. Jensen,[3] Ruth A. Kleinerman,[2]
Hjalgrim S. Jensen,[3] John T. Flannery,[4] *and* Joseph F. Fraumeni, Jr.[5]

ABSTRACT—To lay the groundwork for subsequent chapters in this monograph of multiple primary cancers in Connecticut and Denmark, we present a description of the historical significance of previous studies, focusing on key surveys that have enhanced our understanding of the origins of multiple cancers. Case reports, hospital series, and cancer registry studies have progressively sharpened our perspective on the patterns and causes of multiple cancers. These findings in turn have generated hypotheses about host and environmental determinants of various combinations of cancer and have provided clues to the actual mechanisms of carcinogenesis. The registries of Connecticut and Denmark which began in the 1930s and 1940s, respectively, afford investigators a unique opportunity to analyze the cancer experience of well-defined populations, followed for long periods. The major contribution of this monograph is the evaluation of second cancer risks among long-term survivors of cancer, including relatively rare tumors about which little information currently exists. For patients with a particular cancer, the number of observed second cancers are tabulated over time and compared with those expected if the patients experienced the same rates prevailing in the corresponding general population. We have discussed problems in distinguishing statistical artifacts from biologically plausible associations in light of the potential biases inherent in follow-up surveys of cancer patients; for example, heightened medical surveillance and mistaken metastases could result in false indications of elevated risk. Several differences in the reporting, follow-up, and coding practices between the Connecticut and Denmark registries are described and probably account for many differences in the reported findings. It is hoped that this monograph will stimulate further research into multiple cancer syndromes that will provide insights to the causes of cancer and to strategies for prevention.—Natl Cancer Inst Monogr 68: 3-9, 1985.

For over 100 years, it has been recognized that the tendency to multiple primary cancers in some individuals provides a clue to the understanding of cancer etiology. The risk of developing more than 1 primary cancer in a single patient may be linked to underlying environmental exposures, such as tobacco smoking (*1*), or to host susceptibility factors, such as immunodeficient states (*2*). In addition, the identification of multiple cancer syndromes has generated insights into carcinogenic mechanisms including host–environmental interactions (*3*). Although evaluation of potentially adverse effects of cancer treatment has been useful in the past, generally these were confined to rare events such as lymphangiosarcoma in postmastectomy lymphedema (*4*) or osteogenic sarcoma following orthovoltage radiotherapy (*5*). With the advent of aggressive combined-modality cancer therapy (*6*), including high-voltage radiotherapy and combination chemotherapy with alkylating agents, significant numbers of patients are now living longer periods and may be prone to new malignant tumors as a result of such treatment. The evaluation of second primary cancers also identifies groups of cancer patients in need of increased surveillance aimed at early cancer detection and management and focuses preventive measures to reduce the occurrence of subsequent cancer incidence and mortality.

The two oldest cancer registries (in continuing operation) in the world, Connecticut (1935) and Denmark (1942), provide investigators with an opportunity to evaluate the risk of second cancers among large numbers of persons who have been followed for long periods, often a lifetime. This volume was prepared with several objectives in mind: We hoped to 1) clarify the patterns of multiple primary neoplasms through systematic evaluation of all tumors developing in Connecticut and Denmark during the past 40 to 50 years, including the risk of second cancers among long-term survivors, 2) formulate hypotheses to explain the multiple tumor complexes utilizing available clinical, epidemiologic, or experimental observations, 3) identify groups at especially high or even low risk of second cancer to gain insights into carcinogenic mechanisms or host–environmental interactions, and 4) suggest strategies for future research and preventive actions.

HISTORICAL REVIEW

In 1889, Billroth [cited in (*7*)] reported on the phenomenon of 2 or more independent tumors arising in the same patient and established criteria for the diagnosis of multiple primary cancers. With the improvement in histopathology over the years and an increased number of case reports, Warren and Gates (*8*) summarized the literature on 1,259 well-documented individuals reported to have

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ABBREVIATIONS: NHL = non-Hodgkin's lymphoma; ANLL = acute nonlymphocytic lymphoma; RR = relative risk(s); NOS = not otherwise specified.

[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Radiation Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3A22, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* John D. Boice, Jr., Sc.D.

[3] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark.

[4] Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut 06106.

[5] Epidemiology and Biostatistics Program, Division of Cancer Etiology.

multiple cancers and formulated standards that came to be generally accepted: 1) Each cancer must present a definite picture of malignancy, 2) each must be distinct, and 3) the possibility that 1 cancer represents a metastases from the other must be excluded.

Early studies of multiple cancers consisted mainly of individual case reports. Although detailed criteria were provided to assist physicians in distinguishing metastatic lesions from new primary cancers, little information was included on the magnitude of the occurrence of second tumors among cancer patients. Further advances came when the experience of large hospitals was assembled, such as the Mayo Clinic (*9, 10*), where distinctions were made between cancers of multifocal origin (e.g., multiple carcinomas of the colon or bilateral breast cancer) and cancers of different tissues or organs. More recently, hospital-based cohort studies from the Memorial Sloan-Kettering Cancer Center (*1, 11–13*), the Charity Hospital of New Orleans (*14–16*), and the Princess Margaret Hospital in Ontario (*17*) provided for the first time actual estimates of the risk of developing second cancers among patients with specific tumors. These studies clarified whether certain combinations of cancer occurred excessively or represented chance events. Although hospital-based studies had the advantage of diagnostic refinements, they were often limited by the relatively small number of patients with multiple primaries available from a single institution, which resulted in unstable risk estimates. In addition, potential biases were sometimes introduced by specific referral patterns, treatment practices, local environmental factors, and demographic variation. Therefore, the pattern of second cancer risks for a particular hospital was not always directly applicable to other areas or to cancer patients in the general population.

These difficulties were overcome, in large part, with the establishment of large population-based cancer registries in the 1930–1950s, e.g., Connecticut Tumor Registry (1935) in the United States, Birmingham Cancer Registry (1936) in the United Kingdom, Alberta Cancer Registry (1941) in Canada, Danish Cancer Registry (1942), Cancer Registry of Norway (1953), and others. Monitoring of the cancer experience of well-defined groups followed for a long time then became possible. Surveillance of the cancer incidence and mortality experience of particular geographic areas and entire countries allowed estimates of the risk of second tumors developing in relatively large and unselected populations of cancer patients. Epidemiologists used these data to determine if the presence of a particular cancer placed an individual at higher, lower, or the same risk of developing a second particular cancer compared with persons in the general population of the same age, sex, and race.

Schoenberg and colleagues (*18–21*) published extensively on the value of the population-based tumor registry in studies of multiple cancers. His survey of multiple cancers in Connecticut, 1935–64, appears to be the first comprehensive and quantitative analysis of the risk of second cancers among patients from a well-defined population (*20*). He characterized the risk of subsequent primary cancer by organ site, sex, and time between first and second cancers. Among 120,195 cancer patients, there was overall a significant 29% excess risk of their developing a second primary cancer.

ETIOLOGY OF MULTIPLE CANCERS

The study of multiple primary cancers has led to the identification of tumor constellations which are grouped in text-table 1 according to possible etiologic interpretations. Some of the tumor complexes can be easily explained, whereas others require further investigation for identification of the responsible mechanisms.

Tobacco and Alcohol

Tobacco smoking is clearly one of the major causes of second cancers as it is for first cancers (*22*). Previous studies of second tumors among patients with lung cancer have found excess cancers of the oral cavity, larynx, bladder, cervix, and other tobacco-related sites (*1, 17, 20, 23–25*). The combined effects of tobacco and alcohol account largely for the constellation of cancers arising in the oral cavity, larynx, and esophagus. The risks of developing a second tobacco- or alcohol-related cancer have been linked mainly to the patients' habits prevailing before the onset of the initial cancer, although continued smoking and drinking may enhance the risk (*24*).

TEXT-TABLE 1.—*Etiologic factors involved in multiple primary cancers*

Etiologic factors	Associated cancer sites
Environmental, endocrine, or genetic risk factors	
Tobacco or alcohol consumption, or both	Cancers of the respiratory and upper digestive tracts
Endocrine or dietary factors, or both	Multicentric cancers of the colon; bilateral breast cancer; and clusters of cancers of the breast, uterine corpus, ovary, and colon
Genetic predisposition	Retinoblastoma and osteosarcoma, among others
Treatment effects	
Radiation	Cancer of the rectum following cervical cancer, among others
Chemotherapy	ANLL following Hodgkin's disease, NHL, multiple myeloma, and cancers of the ovary, breast, gastrointestinal tract, and lung, and childhood cancers
Hormones	Cancer of uterine corpus following breast cancer
Immunologic defects	Melanoma following chronic lymphocytic leukemia, among others

Endocrine and Dietary Factors

The constellation of multiple cancers of the breast, uterine corpus, ovary, and colon has long intrigued investigators (*3, 12, 18, 26-28*). Because reproductive factors (e.g., nulliparity) and dietary habits (e.g., high fat intake) appear involved in these cancers, some think that nutritional and hormonal interactions may contribute to the development of multiple primaries of these sites (*29, 30*).

Genetic Predisposition

Although it is unlikely that hereditary cancers contribute substantially to the overall incidence of second tumors among cancer patients, some complexes of tumors result from genetic factors. The association between bilateral retinoblastoma and osteosarcoma illustrates the influence of hereditary factors (*31*). Genetic predisposition may also contribute to the tendency to multicentric cancers arising in the colon and bilateral breast cancer, which are associated with a tendency to familial aggregation. Certain families appear prone to developing cancers of diverse sites (e.g., adenocarcinomas of colon and endometrium, soft tissue sarcomas and breast cancer), with multiple primaries occurring at an early age in some family members (*32*). Genetic–environmental interactions are illustrated by the high risk of radiogenic sarcomas in hereditary forms of retinoblastoma and in the cancer family syndrome described by Li and Fraumeni (*33*).

Treatment Effects

During the last 20 years, the number of cancer patients treated with radiation and chemotherapy has increased, and the study of therapy-related second cancers has become more important (*34, 35*). Children treated with radiotherapy have been reported at high risk of second cancers (*36, 37*), although the risk of subsequent leukemia is not affected by radiation (*38*). Cervical cancer patients exposed to high-dose radiotherapy are prone to cancers of the rectum and other sites with substantial radiation exposures (*39*). In this group, a significantly low rate of breast cancer appears due, in large part, to a protective effect resulting from ovarian ablation. Radiotherapy increases the risk of leukemia following relatively low-dose total body irradiation for NHL (*40*), and of osteosarcomas following high-dose radiotherapy for Ewing's sarcoma (*41*) and retinoblastoma (*31*). Soft tissue sarcomas also appear to be a rare consequence of high-dose radiotherapy for cancer (*5*). Estrogen therapy and ovarian radiotherapy for breast cancer have both been related to an increased risk of endometrial cancer (*42, 43*). Alkylating agents have been associated with extremely high risks of subsequent ANLL following treatment for cancer of the ovary (*44*), gastrointestinal tract (*45*), breast (*46*), multiple myeloma (*47*), lung (*48*), Hodgkin's disease (*49, 50*), NHL (*40*), and childhood cancers (*37*). Cyclophosphamide, an alkylating agent, has been associated with bladder cancer as well as chronic cystitis (*51*).

Immunologic Defects

Certain cancers are complicated by immunodeficiency states which appear to predispose to certain cancers. For example, skin cancers (melanoma and nonmelanoma) have occurred excessively after chronic lymphocytic leukemia (*2*). An increase of NHL following Hodgkin's disease has been linked to the immunosuppressive effects of combination chemotherapy and radiotherapy (*52*). Excess cancers, in particular NHL, have occurred excessively in organ transplant recipients treated with immunosuppressants (*53*).

Obscure Mechanisms

A number of associations have been reported without apparent explanation. For example, cancers of the breast and salivary gland have clustered in several (*54–56*) but not all studies (*57, 58*), and leukemia has occurred excessively following cancer of the testis (*20*), but the reasons for these associations are uncertain.

STUDY POPULATIONS AND ANALYTICAL METHODS

The same rules for selection of study subjects and methods of analyses were applied to data from the Connecticut and Danish Cancer Registries. All persons diagnosed with an invasive cancer between 1935 and 1982 in Connecticut or between 1943 and 1980 in Denmark who survived at least 2 months were followed so that their risk of a second invasive cancer could be determined. Person-years at risk were accumulated for each individual beginning 2 months after the initial cancer diagnosis and ending with the date of death, date last known alive, end of study date, date lost to follow-up, or date of second primary cancer diagnosis, whichever occurred first. Patients with a second cancer diagnosed within the first 2 months of follow-up were considered to have 2 simultaneous cancers and were excluded from the analysis; frequency counts and a brief discussion of these cases are provided in the Connecticut introductory chapter (*59*) and the Danish summary chapter (*60*). Approximately 710,000 patients were included in the study: 330,000 from Connecticut and 380,000 from Denmark. More than 28,000 persons remained at risk after 20 years of follow-up.

Under the assumption that these patients experienced the same cancer incidence as prevailed in the corresponding general population, we obtained expected numbers of second primary cancers by applying the 5-year age, 5-year calendar period, and sex-specific incidence rate for each cancer to the appropriate person-years at risk (*61*). The RR were taken as the ratio of observed-to-expected numbers of second cancers. Tests of significance and 95% confidence intervals for the RR were calculated with the use of an accurate asymptotic approximation to the Poisson distribution (*62*). Testing for linear trend of increasing RR with increasing time since initial cancer diagnosis was conducted according to the method of Breslow et al. (*63*).

PRESENTATION OF RESULTS

Results for each cancer registry are discussed separately in 9 chapters, each covering a major organ system. Cancer sites were grouped according to the World Health Organization's International Classification of Disease, Seventh Revision (*64*). Complete definitions of the cancer site groups used in the monograph for both Connecticut and Denmark data are given in Appendix I. The chapters begin with background information on the initial cancer that might be useful in one's understanding of the pattern of second cancers observed, such as major risk factors, survival figures, usual therapy, and key findings from previous studies of multiple cancers. Second cancer risks are described and then discussed in relationship to possible risk factors and mechanisms and potential sources of biases. At the end of each chapter are tables which present the second cancer risk by sex and by interval since diagnosis of the initial cancer (<1 yr, 1–4 yr, 5–9 yr, 10+ yr, and total). In addition, tables for each cancer site include the percent of first and second cancers which were microscopically confirmed and the proportion of patients who received radiotherapy as part of their first course of treatment. For Connecticut only, tabulations of risk are presented when informative by radiotherapy and by extended latency for long-term survivors. Each Registry concludes with a summary of the major findings, including their implications to the broader issues of cancer etiology and prevention.

DIFFERENCES BETWEEN DENMARK AND CONNECTICUT

Although the Connecticut and Danish Registries have been actively involved in epidemiologic research for many years (*20, 65*), differences exist with regard to reporting, follow-up, and coding practices. For example, the staff of the Connecticut Tumor Registry actively searches hospital files for cases, in addition to receiving notification from clinicians and information on cancer deaths (*59*). It is mandatory in Connecticut that all cancers be reported to the Registry. The Danish Cancer Registry, on the other hand, relies on voluntary notifications by physicians, plus linkage with death certificates (*66*). Although this approach has been found to give a high completeness of reporting of first cancers (*67*), there are indications that second cancers may be underreported in Denmark as found for second leukemia after multiple myeloma (*68*) and solid tumors after cancer of the cervix uteri (*69*). The Danish Cancer Registry, in contrast to the Connecticut Tumor Registry, generally does not report or tabulate multifocal tumors occurring within the same site or in paired organs as it considers it difficult to distinguish new primary cancers within the same organ from recurrence and metastatic spread. For example, data from Connecticut indicate a substantial excess of second breast tumors following an initial breast cancer (*70*), and a substantial number of second colon cancers following an initial colon cancer (*20*). Special care must be taken by the reader when comparing data from the 2 Registries because differences in risk estimates might reflect particular reporting and recording practices rather than variation in etiologic factors.

Radiotherapy is considered to be well documented in records of the Connecticut Tumor Registry, but notations may be incomplete in Danish Cancer Registry files (*69*). Chemotherapy tends to be underreported in both Registries. In Connecticut, chemotherapy is commonly initiated in a physician's office and not necessarily recorded in hospital records. Second cancer risks following chemotherapy were not tabulated in this monograph because of the potential for incomplete ascertainment.

Registration and coding practices also varied with respect to cancers of the bladder, uterine corpus, and brain and central nervous system. Denmark includes papillomas of the renal pelvis, ureter, bladder, and urethra with cancers of the lower urinary tract, and histologically benign tumors of the central nervous system and meninges are grouped with malignant tumors of these sites (*66*). In Connecticut, papillomas and benign brain tumors are not included with the invasive cancers. A special study of cancers of the uterus, NOS, in Connecticut indicated that most originated in the corpus and not the cervix (*71*). Thus the NOS category is included with first primary cancer of the uterine corpus in Connecticut, but it is excluded in Denmark where less than 2% are unspecified. Other differences between Connecticut and Denmark with regard to tabulated data are outlined in the introductory chapters (*59, 66*) and in Appendix I.

CAUTIONS IN INTERPRETATION

When interpreting the results from studies of second primary cancers, one should be mindful of special issues and sources of bias. For a second primary cancer to be classified correctly, a metastatic lesion or local recurrence of the original primary cancer must be excluded as a possible occurrence. Surgery for a first cancer may alter the risk of subsequent cancer for certain organs, e.g., the uterus might be surgically removed during the treatment for cervical cancer and thus not at risk for second cancer development. In addition, because the material analyzed from Connecticut and Denmark was collected over a period of almost 50 years, differences in the distribution of second cancers may reflect changing cancer registration practices over time that determine the completeness and validity of data analyzed. The trends may also be affected by variations in environmental exposures and methods of treatment. The frequency of autopsies among cancer patients also would influence the reported number of second tumors. Moreover, patients with cancer differ in many respects from the general population, and these characteristics may affect the risk of subsequent cancers. For example, women with cervical cancer tend to smoke more, bear children at an earlier age, and are of lower socioeconomic status compared with women in the general population (*72*). Conclusions based upon treatment records in the Registries must be interpreted cautiously because it appears that patients classified as "nonexposed" on the basis of information available in cancer registry records may actually have received radiotherapy and other treatments (*34, 39*). Finally, it should be stressed that one should not use these data to evaluate the efficacy of different treatment regimens, which were not collected in the context of a controlled clinical trial. The low frequency of treatment-induced cancers should not be considered as an indicator of therapeutic success.

Medical Surveillance

Because cancer patients are under close medical scrutiny during the first few years after diagnosis, second cancer diagnosis may be advanced in time, i.e., detected before the tumor would normally become clinically apparent. Also, indolent tumors might be discovered which otherwise would remain dormant and not come to medical attention. For example, thyroid cancer is often detected as a result of medical screening. Prostate cancer is especially susceptible to detection following medical surveillance or as a result of autopsy investigations. In Connecticut, underreporting of second cancers may occur among long-term survivors because of their migration from the state. This factor appears to be of minor importance in Denmark (*66*).

Assessment of Metastases

Although the Registries apply strict criteria before accepting a lesion as a second primary cancer, it is still possible that metastases detected shortly after the diagnosis of an initial cancer may be incorrectly classified as a new primary tumor. A misdiagnosed metastasis is especially likely during the first few years of follow-up, when metastatic spread of the initial cancer occurs most frequently. Conversely, a new primary cancer may be inappropriately classified as metastatic and excluded simply because it occurred at a site where metastases are common. Lung metastases occur in many cancer patients, and it can be particularly difficult for physicians to establish whether subsequent cancer in the lung is primary or metastatic. However, the frequency of metastatic lesions is likely to decrease with time following diagnosis of the initial primary cancer. For some sites, the problem of misdiagnosed metastases is small, especially when the histologic types of the first and second cancers are clearly different.

CONCLUSION

The publication of this monograph is planned to coincide with the Fiftieth Anniversary of the Connecticut Tumor Registry that will be highlighted at the Annual Meeting of the International Association of Cancer Registries to be held in Hartford, Connecticut, in 1985. The data presented here are descriptive and intended more to raise questions than to answer them. Why are certain persons at high risk of developing a second cancer? Why are some at low risk? Why do differences exist in the patterns of multiple cancer in different populations? What environmental and host factors, therapeutic agents, and medical care practices contribute to the development of multiple primaries? What areas should be pursued further with analytic studies? What groups should be screened for early detection of particular cancers? What measures can be taken to reduce the morbidity and mortality associated with subsequent tumors? We hope this volume will stimulate the epidemiologic, clinical, experimental, and multidisciplinary research needed to help settle these issues. A better understanding of multiple cancers should yield greater insights into the risk factors and basic mechanisms of carcinogenesis and provide a more sound basis for the management of cancer-prone individuals including the development of protective measures.

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II. Multiple Primary Cancers in Connecticut

Cancer Registration in Connecticut and the Study of Multiple Primary Cancers, 1935–82 [1]

John T. Flannery,[2] John D. Boice, Jr.,[3] Susan S. Devesa,[4] Ruth A. Kleinerman,[3] Rochelle E. Curtis,[3] *and* Joseph F. Fraumeni, Jr.[5]

ABSTRACT—The Connecticut Tumor Registry (CTR) was established in 1941 and is the oldest population-based cancer registry in the world. Since 1935, all malignant tumors have been registered, and cancer patients are followed annually for vital status. Reporting by hospitals of all cancers diagnosed in Connecticut residents became mandatory in 1971. The reporting physician or hospital makes the initial determination as to whether a tumor is an independent primary cancer, recurrent tumor, or metastatic lesion. In addition, the Registry maintains stringent quality control procedures to avoid duplication of cancer reports. The Registry reviews reports of new cancers developing in patients with a previous primary cancer to rule out the possibility of misdiagnosed metastases. Microscopic confirmation of the diagnosis has improved from 49% in 1935–39 to 94% in 1980–82. Cancers reported only from death certificates currently account for only 1% of all registrations. Between 1935 and 1979, cancer rates in Connecticut almost doubled among males and increased by more than one-third among females; notable increases were seen for cancers of the lung and prostate in males and cancers of the lung and breast in females. In recent years, rates for malignant melanoma of the skin have increased dramatically among both sexes. Stomach cancer has decreased over time in both sexes, as has cervical cancer in females. Although the CTR has used several revisions of the International Classification of Diseases to code the primary site of cancers, rules for the coding of multiple primary cancers have remained essentially the same. Among 253,536 individuals diagnosed between 1935 and 1982 with an invasive cancer, 16,727 (6.6%) nonsimultaneous second cancers were evaluated and are discussed in subsequent chapters of this monograph. Simultaneous cancers were diagnosed in 4,107 individuals and accounted for approximately 20% of all multiple cancers reported in Connecticut. The most frequent simultaneous tumors were cancers of the colon, rectum, prostate, lung, breast, and bladder. Some simultaneous cancers (chronic lymphocytic leukemia, testis, prostate, rectum, uterine corpus, and liver and biliary tract) occurred almost as frequently as the number of subsequent nonsimultaneous tumors, which suggests that the patterns of risk over time for certain sites may be distorted when diagnoses are advanced in time and removed from analysis. The study of second cancers also involves other problems not inherent to most epidemiologic investigations: Results could be influenced by changes over time in cancer registration or coding practices, by the introduction of new cancer therapies, by misclassification of therapy in registry records, by intense medical surveillance of cancer patients, or by conditions such as metastases and autopsy diagnoses that are critical to the evaluation of second cancers. Nonetheless, the study of multiple primary cancers in a well-defined population, such as in Connecticut, provides a unique opportunity for etiologic research, risk estimation, and hypothesis generation. Such studies also suggest areas for preventive action that warrant close attention by the clinical and scientific community.—Natl Cancer Inst Monogr 68: 13–24, 1985.

In this chapter, we discuss the history of the CTR, coding and registration practices and the evaluation of multiple primary cancers over the years 1935–82. Trends in cancer incidence are presented which show the dynamic nature of cancer occurrence and registration over a period of almost 50 years. Previous studies on multiple primary cancers with CTR data are summarized. An analysis of simultaneous cancers, i.e., those occurring within 2 months of each other, is discussed. The methods the CTR used to evaluate the occurrence of new second cancers in Connecticut residents are described. Finally, the potential pitfalls associated with studies of multiple primary cancers are outlined.

BRIEF HISTORY OF THE CONNECTICUT TUMOR REGISTRY

The concept for a tumor registry in Connecticut evolved from early medical and public recognition of the need for statewide cancer statistics in cancer control. In 1926, a cancer survey was conducted in New Haven (*1*) that led to the formation of the Cancer Committee of New Haven in 1930. This Committee subsequently recommended that cancer rates in Connecticut be continually surveyed and that the public be educated about the early symptoms of cancer and encouraged to seek early diagnosis and treatment. About the same time, physicians in the State formed a Tumor Study Committee and began planning for a statewide registry of hospitalized cancer patients.

ABBREVIATIONS: CTR = Connecticut Tumor Registry; DHS = Department of Health Services (State of Connecticut); SEER = Surveillance, Epidemiology, and End Results (Program); GI = gastrointestinal; NOS = not otherwise specified; ICD (ICD-O) = International Classification of Diseases (for Oncology); ANLL = acute nonlymphocytic leukemia; CLL = chronic lymphocytic leukemia; RR = relative risk(s).

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut 06106.

[3] Radiation Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3A22, National Cancer Institute, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* John D. Boice, Jr., Sc.D.

[4] Biostatistics Branch, Division of Cancer Etiology.

[5] Epidemiology and Biostatistics Program, Division of Cancer Etiology.

In 1935, legislation was enacted which authorized the Connecticut DHS to investigate cancer mortality, treatment, and prevention with the goal of reducing cancer mortality. To this end, the DHS created the Division of Cancer Research in 1935, and from that time until 1941, efforts were directed toward the development of tumor clinics and registries in local hospitals. These efforts laid the groundwork for hospitals to report case histories of cancer patients to the CTR, which was started in 1941. One of the first tasks of the Registry was to collect retrospectively data on all cancer patients admitted to Connecticut hospitals as of January 1, 1935.

Since the late 1950s, the CTR has collaborated with the National Cancer Institute in two large cancer programs. From 1957 to 1972, the CTR and 11 other cancer registries, most of which were hospital based, were part of the End Results Program (*2*). In 1973, the CTR joined the SEER Program (*3*), which gathers information about cancer incidence, survival, and mortality in selected areas of the country. Currently, the SEER Program has more than a decade of cancer registration encompassing close to 12% of the residents in the United States. The CTR continues to participate in the SEER Program and reports data on new cancer cases to the National Cancer Institute on an annual basis.

Cancer Registration

The CTR was established in 1941 in the DHS in Hartford, Connecticut, and is the oldest population-based cancer registry in the world. Since 1935, malignant tumors have been reported to the Registry if diagnosed in a resident of Connecticut. Although the Registry has collected information on basal cell and squamous cell carcinomas of the skin from 1935 through July 1984, this registration is considered incomplete. Reports of all newly diagnosed cancers to the DHS became mandatory in 1971. Each hospital in Connecticut licensed by the DHS is required to submit reports containing data on the diagnosis, pathology, and treatment of the cancer, as well as patient demographic information. The hospitals are also required to submit follow-up information annually for patients diagnosed with malignant tumors.

Field staff from the Registry are responsible for cancer identification and record abstraction at the 2 Veterans Administration Medical Centers in Connecticut and selected out-of-state hospitals where Connecticut residents traditionally go for medical treatment. The CTR is also routinely notified of any Connecticut resident reported to central tumor registries in the States of New York and Massachusetts. Copies of all death certificates with mention of cancer are also supplied by the Vital Records Section of the DHS. These death certificates are routinely linked to registry files, and any that are not matched to a patient already in the Registry are thoroughly evaluated for diagnostic confirmation of cancer. In recent years, less than 2% of all incident cancers were identified only by death certificate notification.

The Registry maintains internally stringent quality control to avoid duplication of cancer reporting and data errors. Quality control measures range from recoding of samples of records to sophisticated data processing-editing procedures. Quality control efforts at the hospital level include cancer case-finding audits and record re-abstracting projects. The CTR has on file over 374,000 malignant tumors diagnosed during the period 1935–82. Currently, more than 87,000 patients are actively followed for vital status.

Area and Population

Connecticut is situated on the northeastern coast of the United States and is bounded by the State of New York on the west, Massachusetts on the north, Rhode Island on the east, and Long Island Sound on the south. The total registration area is 12,973 km^2. The population of Connecticut was 3,107,576 according to the 1980 Federal Census (*4*), with males comprising 48% and females 52% of the population. The median age of the population was 32.0 years in 1980 and the racial composition was 91% white, 7% black, and 2% other.

The population is primarily urban [78% in 1980; (*4*)] and relatively affluent. The average median income is higher than 75% of the other 49 states. Slightly over one-half of the working population is employed in professional or managerial occupations, and the balance is employed in skilled or semiskilled occupations. Only 0.7% of the population work on farms. The 40 hospitals in Connecticut are spread across the State, and medical care is accessible to all residents. The largest 2 medical centers treat about 20% of all cancer patients in the State.

CANCER INCIDENCE IN CONNECTICUT, 1935–79

From 1935–39 to 1975–79, the average annual age-adjusted (World Standard) incidence among males of invasive cancer of all sites combined increased 88% from 167 to 314/100,000 population in Connecticut (text-table 1). About one-half of this increase, however, occurred during the first 15 years of Registry operation, after which time the rate of increase dropped to its current level of about 1% per year. Among females, the overall increase was 35% from 1935–39 to 1975–79, i.e., 194 to 261/100,000/year or generally less than 1% per year (text-table 2).

Different patterns of risk over time are apparent for the various cancers considered. The trends in cancer incidence from 1935 to 1979 among males are presented in figure 1 for the major GI organs. The incidence of colon cancer has more than doubled, with the rate of increase slightly higher before 1955 compared with more recent years. The incidence of rectal cancer, meanwhile, increased during the early years but remained fairly stable after 1950. During 1935–39, stomach cancer was diagnosed almost twice as frequently as colon cancer among males, whereas colon cancer is now more than three times as likely to occur as stomach cancer. Dramatic declines of more than 60% are seen for stomach cancer rates: from 29 to 11 per 100,000 per year between 1935–39 and 1975–79. The incidence of pancreatic cancer increased by 50% during 1935–55 but remained relatively stable thereafter. Because detection of pancreatic cancer is difficult, the early increases may be due partially to improvements in diagnostic tests. The

TEXT-TABLE 1.—*Age-adjusted (World Standard) cancer incidence rates/100,000 population by primary site and year of diagnosis for males, Connecticut, 1935–79*[a]

ICD-O code[b]	Cancer site/type	Yr of diagnosis								
		1935–39	1940–44	1945–49	1950–54	1955–59	1960–64	1965–69	1970–74	1975–79
140	Lip	4.4	4.2	4.9	4.0	4.1	3.5	2.4	2.0	1.5
141	Tongue	2.8	3.0	2.9	3.0	3.1	3.8	2.8	3.2	3.3
142	Salivary gland	0.7	0.4	0.7	0.7	0.7	1.0	1.1	1.0	0.9
143–145	Gum, other mouth	3.8	3.4	3.3	4.1	4.0	4.2	4.1	4.6	4.9
146	Oropharynx	1.1	1.1	1.6	1.8	2.0	2.2	2.1	2.1	2.1
147	Nasopharynx	0.4	0.4	0.5	0.6	0.7	0.6	0.7	0.6	0.7
148	Hypopharynx	0.4	0.7	0.7	1.2	1.4	1.6	1.5	1.5	1.8
149.0,149.1	Pharynx, NOS	0.9	0.8	0.6	0.6	0.4	0.3	0.4	0.3	0.5
149.8,149.9	Buccal, ill defined	0.1	0.1	0.1	0.1	0.0	0.2	0.3	0.2	0.2
150	Esophagus	5.1	5.2	6.6	6.9	7.0	6.0	5.9	5.4	5.8
151	Stomach	29.1	26.3	25.2	21.8	18.4	17.0	13.9	12.4	10.9
152	Small intestine	0.7	0.7	0.7	0.6	0.5	0.8	0.8	0.9	0.7
153	Colon	15.9	18.5	21.1	23.4	26.4	27.5	28.8	30.9	33.8
154.0–154.8	Rectum	14.5	15.7	17.7	18.0	17.5	16.4	17.3	18.0	18.0
155	Liver	3.1	2.3	2.1	1.2	1.9	2.1	2.0	2.0	2.4
156	Gallbladder	1.4	1.5	1.6	2.0	2.1	2.5	2.3	2.0	2.1
157	Pancreas	5.9	5.8	6.7	7.3	8.9	8.9	9.0	8.9	9.1
158	Peritoneum	0.9	0.6	0.5	0.4	0.5	0.4	0.8	0.7	0.4
159	Other digestive	1.9	1.7	1.6	1.0	0.8	0.6	0.5	0.4	0.3
160	Naval cavities, sinuses	0.7	0.7	0.7	0.7	0.6	0.7	0.5	0.7	0.7
161	Larynx	3.4	3.7	5.1	5.4	5.5	7.7	7.8	7.8	8.2
162	Bronchus, lung	8.8	11.6	18.5	27.8	37.8	43.7	51.2	57.6	63.4
163	Pleura	0.1	0.1	0.1	0.1	0.2	0.2	0.3	0.3	0.5
164.1–164.9, 165	Intrathoracic	0.4	0.4	0.2	0.5	0.2	0.2	0.2	0.3	0.3
175	Male breast	0.5	0.6	0.4	0.3	0.3	0.6	0.5	0.7	0.8
185	Prostate	20.4	23.4	25.7	30.4	33.7	36.8	38.1	39.3	45.6
186	Testis	1.5	1.8	2.2	2.1	2.3	2.6	2.7	2.9	3.5
187	Penis	1.3	1.0	1.3	1.2	1.2	1.1	0.8	1.0	0.9
189.0–189.2	Kidney, renal pelvis, ureter	3.0	3.9	4.7	5.4	7.2	7.2	8.2	8.6	9.0
188	Bladder	8.2	8.6	11.8	12.6	14.1	15.7	19.3	21.5	22.2
189.3–189.9	Other urinary	0.0	0.0	0.2	0.2	0.1	0.1	0.3	0.3	0.3
173[c]	Melanoma	0.9	1.1	1.4	1.7	2.2	3.5	4.1	5.4	7.2
190	Eye	0.7	0.4	0.7	0.6	0.8	0.7	0.6	0.6	0.5
191, 192.0, 192.1	Brain	1.5	2.7	3.1	4.3	5.1	5.2	5.2	5.8	6.5
192.2–192.9	Other CNS	0.1	0.1	0.1	0.2	0.3	0.3	0.3	0.2	0.2
193	Thyroid gland	0.2	0.5	0.5	0.9	1.0	1.1	1.6	1.7	2.0
164.0	Thymus gland	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1
194	Endocrine gland	0.2	0.4	0.3	0.5	0.3	0.5	0.3	0.3	0.4
170	Bone	1.5	1.4	1.4	0.9	1.2	0.9	0.9	0.7	0.9
171	Connective tissue	1.4	1.6	1.7	1.7	2.2	2.7	2.4	2.2	2.2
	NHL	3.2	3.2	4.6	6.0	6.2	6.9	7.6	8.3	8.3
	Hodgkin's disease	2.2	2.4	2.4	3.6	3.1	3.8	4.0	4.5	3.6
	Multiple myeloma	0.4	0.5	1.0	1.5	2.3	2.1	2.6	3.2	3.5
	Leukemias, total	4.3	5.6	7.6	8.9	10.1	10.3	9.8	11.9	10.9
	Acute, all types	1.5	1.7	3.0	3.1	3.8	4.4	4.6	5.5	5.0
	ALL	0.7	0.9	1.2	1.0	1.3	1.4	1.4	2.0	1.7
	Acute myelogenous	0.5	0.6	1.2	1.1	1.3	1.3	2.1	2.7	2.5
	Chronic, all types	0.7	1.3	2.1	2.8	3.5	3.4	3.1	4.7	4.3
	CLL	0.4	0.8	1.3	1.8	2.3	2.1	2.1	3.1	2.6
	Other leukemias	2.1	2.7	2.5	3.0	2.8	2.5	2.1	1.6	1.6
195.0–195.8, 199.9[d]	Other, unknown sites	8.4	9.6	10.2	12.2	12.8	11.4	12.8	12.8	12.3
140–195	All sites	166.6	177.6	205.1	228.6	251.6	265.9	278.9	295.4	313.5

[a] *See* (*11*). CNS = central nervous system; ALL = acute lymphocytic leukemia; CLL = chronic lymphocytic leukemia.

[b] Cancers of the lymphatic and hematopoietic system are defined by ICD-O morphology codes (M), as follows: NHL = 9590–9642, 9690–9701, 9740–9750; Hodgkin's disease = 9650–9662; multiple myeloma = 9730, 9731; leukemias, total = 9800–9940; acute leukemias = 9801, 9821, 9841, 9861, 9866, 9891; ALL = 9821; acute myelogenous = 9861; chronic leukemias = 9803, 9823, 9842, 9863, 9893; CLL = 9823; other leukemias = 9800, 9802, 9804, 9810, 9820, 9822, 9824, 9825, 9830, 9840, 9850, 9860, 9862, 9864, 9865, 9870, 9880, 9890, 9892, 9894, 9900–9940.

[c] Melanoma of the skin includes M-8720–8780.

[d] Other and unknown sites also include M-9710–9722, 9950–9970.

TEXT-TABLE 2. *Age-adjusted (World Standard) cancer incidence rates/100,000 population by primary site and year of diagnosis for females, Connecticut, 1935–79*[a]

ICD-O code[b]	Cancer site/type	Yr of diagnosis								
		1935–39	1940–44	1945–49	1950–54	1955–59	1960–64	1965–69	1970–74	1975–79
140	Lip	0.3	0.3	0.2	0.2	0.3	0.2	0.2	0.2	0.2
141	Tongue	0.3	0.4	0.6	0.6	0.6	0.7	0.8	1.1	0.9
142	Salivary gland	0.4	0.5	0.7	0.7	0.7	0.6	0.6	0.8	0.7
143–145	Gum other mouth	0.5	0.8	0.8	1.0	0.8	1.2	1.3	1.5	1.9
146	Oropharynx	0.1	0.2	0.2	0.2	0.4	0.4	0.6	0.7	0.7
147	Nasopharynx	0.2	0.1	0.2	0.3	0.2	0.2	0.1	0.2	0.3
148	Hypopharynx	0.2	0.1	0.1	0.1	0.2	0.2	0.3	0.3	0.3
149.0, 149.1	Pharynx, NOS	0.1	0.2	0.1	0.1	0.0	0.1	0.1	0.1	0.2
149.8, 149.9	Buccal, ill defined	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.1
150	Esophagus	1.3	1.4	1.2	1.1	0.9	1.1	1.4	1.2	1.8
151	Stomach	17.9	14.6	13.6	10.7	9.4	8.1	6.0	5.4	4.9
152	Small intestine	0.4	0.7	0.5	0.7	0.6	0.6	0.6	0.6	0.5
153	Colon	17.9	19.4	24.5	25.4	26.1	26.6	26.0	26.1	25.9
154	Rectum	10.9	11.0	11.6	12.6	12.2	10.9	11.1	11.0	11.6
155	Liver	3.8	2.3	1.3	1.1	0.9	0.9	0.7	0.9	0.9
156	Gallbladder	3.0	2.7	3.1	4.0	3.6	3.0	2.7	2.3	1.9
157	Pancreas	4.6	4.5	4.9	5.0	4.5	5.0	5.4	6.1	5.9
158	Peritoneum	0.6	0.4	0.5	0.6	0.5	0.6	0.6	0.3	0.3
159	Other digestive	2.6	2.1	1.9	0.7	0.7	0.6	0.3	0.3	0.2
160	Nasal cavities, sinuses	0.6	0.5	0.4	0.3	0.4	0.5	0.4	0.4	0.4
161	Larynx	0.3	0.3	0.3	0.2	0.6	0.7	0.9	1.1	1.4
162	Bronchus, lung	2.8	2.4	3.3	4.0	5.1	6.9	9.3	14.6	21.6
163	Pleura	0.1	0.1	0.1	0.0	0.1	0.1	0.1	0.1	0.1
164.1–164.9, 165	Intrathoracic	0.2	0.2	0.0	0.0	0.1	0.1	0.1	0.1	0.2
174	Female breast	47.7	48.5	53.6	58.1	58.4	62.2	69.0	75.8	78.0
180	Cervix	18.8	16.7	17.7	16.3	15.3	12.2	10.7	9.7	7.9
182	Corpus uteri	6.4	7.3	9.5	11.9	13.3	14.8	15.3	19.2	20.6
179	Uterus, NOS	10.8	8.5	7.5	6.5	4.8	2.8	1.9	1.1	0.6
183	Ovary, fallopian tubes	10.5	11.4	11.1	12.6	12.5	12.7	12.8	12.7	12.0
184	Other female genital	2.5	2.3	1.6	2.0	1.9	1.9	2.0	1.8	1.8
181	Placenta	0.0	0.1	0.3	0.0	0.1	0.1	0.1	0.1	0.0
189.0–189.2	Kidney, renal pelvis, ureter	2.0	2.1	2.9	3.0	3.2	3.5	3.4	3.6	4.4
188	Bladder	3.7	3.3	3.7	3.9	3.6	4.2	4.9	5.4	6.4
189.3–189.9	Other urinary	0.1	0.2	0.1	0.1	0.2	0.1	0.1	0.2	
173[c]	Melanoma	0.7	1.2	1.5	2.1	2.4	3.2	4.1	4.5	6.3
190	Eye	0.4	0.6	0.6	0.8	0.5	0.8	0.5	0.5	0.5
191, 192.0, 192.1	Brain	1.3	1.5	2.4	3.0	3.5	3.8	4.1	3.5	4.3
192.2–192.9	Other CNS	0.0	0.2	0.1	0.3	0.1	0.3	0.3	0.2	0.2
193	Thyroid gland	1.0	1.0	1.3	2.6	2.7	3.3	3.4	3.8	4.5
164.0	Thymus gland	0.0	0.0	0.0	0.1	0.0	0.2	0.1	0.1	0.1
194	Endocrine gland	0.1	0.3	0.2	0.3	0.2	0.4	0.2	0.2	0.4
170	Bone	1.1	1.2	1.2	0.8	0.7	0.7	0.8	0.6	0.6
171	Connective tissue	1.3	1.5	1.3	1.6	1.6	1.8	1.5	1.6	1.3
	NHL	1.7	2.6	3.2	4.3	5.1	5.0	5.6	5.6	6.8
	Hodgkin's disease	1.4	1.3	1.8	2.2	2.3	2.4	3.2	2.7	3.0
	Multiple myeloma	0.4	0.3	0.8	1.4	1.5	1.9	1.8	2.6	2.8
	Leukemias, total	4.1	4.6	5.3	5.9	6.4	6.5	5.9	6.9	6.6
	Acute, all types	1.3	1.7	2.0	2.9	2.9	3.3	3.1	3.9	3.5
	ALL	0.6	0.8	0.8	1.0	0.9	1.1	0.9	1.3	1.1
	Acute myelogenous	0.5	0.6	0.7	1.1	0.9	1.1	1.5	2.1	1.9
	Chronic, all types	0.8	0.8	1.3	1.4	2.0	1.8	2.0	2.3	2.3
	CLL	0.4	0.4	0.6	0.7	1.1	1.0	1.2	1.4	1.4
	Other leukemias	2.1	2.1	2.1	1.6	1.5	1.4	0.9	0.7	0.9
195.0–195.8, 199.9[d]	Other, unknown sites	8.2	8.8	8.8	9.5	9.9	8.5	8.5	9.0	9.2
140–195	All sites	193.6	190.6	206.7	219.0	219.3	222.5	230.0	246.4	261.4

[a] *See* (*11*). *See* text-table 1 for definitions.

[b] *See* footnote *b* in text-table 1.

[c] *See* footnote *c* in text-table 1.

[d] *See* footnote *d* in text-table 1.

incidence of esophageal cancer also has been relatively stable during the past two decades. Cancers of the liver and gallbladder occur considerably less frequently than do other GI tumors, and incidence rates have not changed substantially since the late 1950s. From 1935 to 1955, the frequency of gallbladder cancer increased, whereas liver cancer decreased.

Among non-GI cancers, the largest increase in cancer incidence over time among males was for the lung: The incidence rate during the late 1970s was more than seven times that during the late 1930s (fig. 1). The rate of increase was particularly steep from 1940 to 1959. During the 1970s, lung cancer rates have been higher than those of any other primary cancer and have continued to climb at about 2% per year. To a lesser extent, the incidence of laryngeal cancer also increased. Prostate cancer is the second most frequent cancer among males, and the reported incidence rate more than doubled over the entire period. This rise may be due in part to an increase in the detection of clinically occult lesions of the prostate (*5*). Two major cancers within the urinary system have increased over time: Rates for urinary bladder cancer rose over the same period, whereas the rate of increase for kidney cancer was most pronounced prior to 1960. Although skin melanoma was uncommon in the early years of Registry operation, the incidence has risen dramatically to surpass the rate of increase reported for lung cancer. The overall rates for cancers of the buccal cavity and pharynx, which include a diversity of subsites, have remained relatively constant; substantial decreases in lip cancer were recorded, whereas some other sites showed upward trends. Increasing rates were also apparent for cancers of the brain, testis, and thyroid.

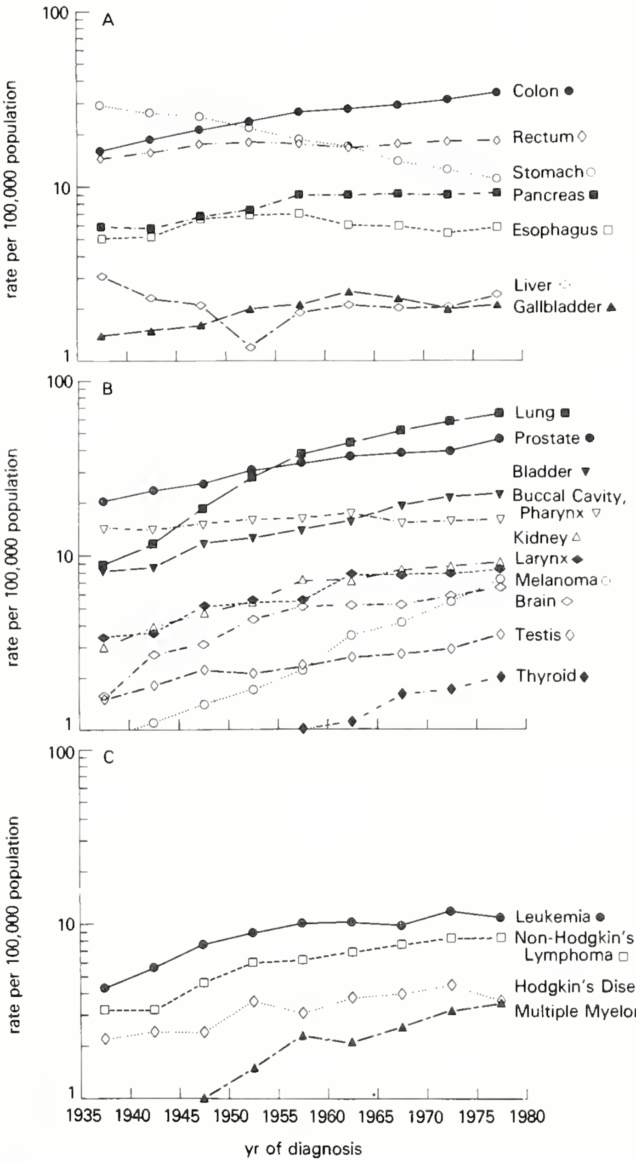

FIGURE 1.—Age-adjusted cancer incidence trends among males in Connecticut, 1935–79. A) GI sites, B) non-GI sites, C) lymphatic and hematopoietic sites.

The incidence trends for lymphatic and hematopoietic cancers are presented in figure 1. Increases are observed for each type, with multiple myeloma being most pronounced. The increase in Hodgkin's disease was most notable from the late 1940s to the early 1950s, but since then the rates have not shown consistent trends. The rates for non-Hodgkin's lymphomas increased by more than 150% between 1935 and 1979, although the rate of increase was less in recent years. The incidence rates for the leukemias have also increased substantially, by more than 150%, most noticeably during the early years of the CTR operation.

The trends in cancer occurrence have also varied considerably among females. Colon cancer occurs more frequently than any other GI cancer, and after increasing from 1935 to 1949, incidence rates have remained relatively constant (fig. 2). The incidence of rectal cancer has also been relatively stable over the last 45 years. Stomach cancer, which was as common as colon cancer in 1935–39, has decreased substantially and at a rate comparable to that observed among males. The incidence of pancreatic cancer among females has increased slightly, whereas rates for gallbladder cancer increased until 1955 and have been decreasing ever since. Although the incidence of esophageal cancer is low among females, incidence rates did not show large changes until 1975–79 when rates were seen to rise. Liver cancer is rare in women, and incidence rates have remained consistently less than 1 per 100,000 per year since the late 1950s, after declining dramatically from 1935 to 1955.

Incidence rates for many non-GI cancers are considerably lower among females than among males (fig. 2). However, the rates of lung cancer have shown more dramatic increases among females than among males: from 2.8 to 22/100,000 between 1935–39 and 1975–79. The rate of increase has accelerated with time and in the late 1970s was greater than 8% per year. The reported incidence of skin melanoma also rose sharply, from 0.7 to 6.3/100,000 during 1935–39 to 1975–79. Cancers of the urinary bladder and kidney have also increased but at lower levels. Increases in cancers of the buccal cavity and pharynx occurred during the early years of Registry operation and then after about 1955. In contrast to males, the rates for lip cancer among females have been consistently low. Sub-

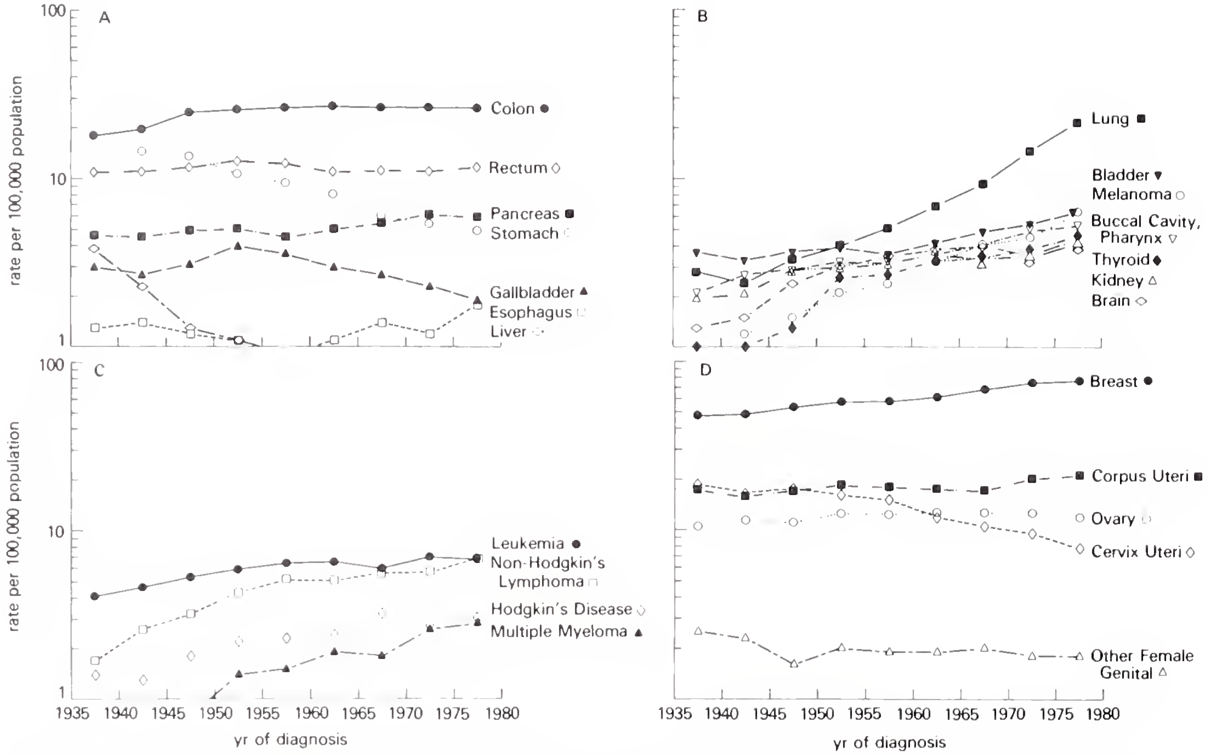

FIGURE 2.—Age-adjusted cancer incidence trends among females in Connecticut, 1935–79. A) GI sites, B) non-GI sites, C) lymphatic and hematopoietic sites, D) breast and female genital sites.

stantial increases over time were apparent for cancers of the brain and thyroid.

Breast cancer is by far the most frequent cancer among females, and the incidence rate has been increasing over time (fig. 2). In contrast, the incidence of invasive cancer of the cervix uteri has declined by 58%, from 19 to 7.9/100,000 between 1935–39 and 1975–79. The rates for cancer of the corpus uteri (including uterus, NOS) showed only modest variations between the late 1930s and the late 1960s, but increases occurred during the 1970s and then declined. The incidence of ovarian cancer has been stable, especially since the early 1950s.

Trends for lymphatic and hematopoietic cancers among females are shown in figure 2. As in males, the diagnosis of multiple myeloma has increased sharply among females, with some increases also seen for Hodgkin's disease. Incidence rates for the non-Hodgkin's lymphomas rose substantially from the late 1930s to the late 1950s, but subsequent increases were only moderate. Leukemia rates have changed little since 1960, despite increases in earlier periods.

In conclusion, increasing trends have been observed in the incidence of many primary cancers among both males and females in Connecticut from 1935 to 1979, whereas other tumors have shown declining rates. The increases seen during the early years of the Registry may be due partially to special efforts on the part of the CTR to improve case-finding and reporting. Increases over longer periods may be partly indicative of improvements in medical care and diagnosis. However, temporal variations over many years or even a short time could reflect changes in the prevalence of various risk factors. For example, the proportion of the population composed of long-term smokers who are at risk of developing lung cancer has increased significantly over time, especially among women (*6*). The increase in cancer of the corpus uteri during the 1970s appeared to result from the use of menopausal estrogens (*7*). Thus some trends, at least since the late 1940s, probably indicate real changes in the risk of various cancers among Connecticut residents and not artifacts associated with reporting practices or the accuracy of diagnostic tests. Comparisons of the Connecticut data with those available from other areas of the country, although available for many fewer years than in Connecticut, indicate regional differences in cancer incidence among whites that vary by primary cancer (*8*); however, some uncertainties regarding the accuracy of the earlier data could be inferred from all geographic areas. In the past, nonwhites comprised a low proportion of the population in Connecticut; over the years, increasing numbers of blacks and other ethnic groups have moved into the State. To the extent that the risk of cancer among nonwhites may differ from that among whites, the rates for all races combined will be altered. Incidence rates for many cancers among nonwhites have tended to increase more rapidly than among whites (*9*); this may also partially explain some of the observed incidence trends.

Microscopic Confirmation

The percent of microscopically confirmed cancers reported to the CTR has increased steadily over time, from

49% of all tumors in 1935–39 to 94% in 1980–82 (text-table 3). About 2% of all cancers were microscopically confirmed only at autopsy. Such cancers may not be associated with any recognizable symptoms prior to death, and changes in the frequency of autopsy rates over time could affect the reported incidence rates. In contrast, the proportion of cancers reported only on the basis of a death certificate, i.e., cancers for which follow-back information was not available, has decreased over time. Diagnoses made only on the basis of death certificates accounted for about 40% of cancers which were not microscopically confirmed. Such diagnoses are not always accurate, although this appears to be less of a problem for cancer diagnoses compared with other causes of death (*10*). Since 1960, approximately 5–7% of all cancers were clinical or surgical diagnoses that were not microscopically confirmed.

Coding Changes From 1935 to 1982

Throughout its operation, the CTR has used 6 coding schemes to classify cancer diagnoses. Their coding modifications were made to increase the specificity of classifying primary cancers, to be compatible with other organizations collecting and reporting cancer data, and to be comparable with death certificate coding practices (*11*). The earliest scheme used from 1935 to 1948 consisted of a 3-digit site and 3-digit histology code created by the CTR. The Sixth Revision of the ICD (*12*) superseded the CTR codes (1949–56) and was subsequently replaced by a modified Seventh Revision (1957– 67) (*13*). From 1968 through 1974, the ICD-7 codes continued to be used with additional Eighth Revision titles. In 1975, these codes were converted to SEER codes (*14*) which were based on the Ninth Revision of the ICD. In 1977, the site and histology designations for all cancer cases were converted to ICD-O (*15*), and this scheme has remained in use through the present.

Site Groups Used in This Monograph

The ICD-O site groups used throughout this monograph conform with SEER rules, which differ slightly from those used by the CTR (*11*) and as presented in tables 1 and 2. For example, melanoma of an unknown primary site is assumed by SEER to be melanoma of the skin (ICD-O, 173; morphology 8720–8780); cancer of the thymus (ICD-O, 164.0) is grouped with cancer of other endocrine glands (ICD-O, 194). In addition, intestinal tract, NOS (ICD-O, 159.0) is grouped with colon cancer (ICD-O, 153).

Urinary bladder papillomas have been reported to the CTR since 1957 and are coded as benign by the Registry. Connecticut does not include papillomas in the rates for bladder cancer, whereas they are included in the Danish Cancer Registry data (*16*). Rates for uterus, NOS, have declined steadily over time, and a special study of these NOS cancers in Connecticut has indicated that most originated in the corpus and not the cervix (*17*). Therefore, initial cancers of the uterus, NOS, have been grouped with those of the uterine corpus in the Connecticut portion of this monograph; in contrast, Denmark has maintained separate categories. The CTR calculated rates for ANLL by combining acute myelogenous and monocytic leukemias, erythroleukemia, and acute leukemia, NOS.

MULTIPLE PRIMARY CANCERS IN CONNECTICUT

The CTR has been a member of the SEER Program of the National Cancer Institute since 1973 and follows the SEER guidelines that pertain to multiple primary cancers (*14*). Prior to 1973, rules and definitions used by the CTR for multiple primaries were basically the same as those adopted by the SEER Program. The CTR defers to the reporting physician or hospital pathologist as to whether a tumor is an independent primary cancer, a recurrent cancer, or a metastatic lesion. However, reports of new cancers developing in patients with previously reported primary cancers are independently reviewed by the Registry, and questionable cases are referred back to the reporting physician or hospital for further investigation.

Definitions of Multiple Primary Cancers in Connecticut

The following definitions and coding rules are used for multiple primary cancers in Connecticut:

TEXT-TABLE 3.—*Percent distribution of method of confirmation for all cancers by year of diagnosis for males and females in Connecticut, 1935–82*

Confirmation	Yr of diagnosis										
	1935–39	1940–44	1945–49	1950–54	1955–59	1960–64	1965–69	1970–74	1975–79	1980–82	All years
	No. of cancers in interval										
	15,898	18,956	23,461	28,727	34,254	39,102	44,642	51,574	59,344	38,153	354,111
Microscopically confirmed											
Surgical/other	47.6	57.0	67.0	74.4	77.9	82.5	86.8	89.4	92.0	92.6	81.7
Autopsy only	1.1	1.3	1.7	2.2	2.6	3.6	3.5	2.1	1.4	0.9	2.1
Not microscopically confirmed											
Clinical/surgical	16.2	16.5	13.6	9.6	8.6	8.9	7.7	7.1	5.5	5.2	8.6
Autopsy only	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.2	0.0	0.0	0.1
Death certificate	35.0	25.2	17.6	13.8	10.8	5.0	2.0	1.2	1.2	1.3	7.5

1) Site: For colon, rectum, bone, connective tissue, and skin, each subcategory as delineated in the ICD-O is considered to be a separate site. For all other sites, each category as delineated in the ICD-O is considered to be a separate site. For example, transverse colon (ICD-O site code 153.1) and descending colon (153.2) are considered to be separate sites, whereas trigone of urinary bladder (188.0) and lateral wall of urinary bladder (188.2) are considered to be subsites of the urinary bladder. Each side of a paired organ is considered to be a separate site unless metastatic. A lymphoma is coded to an extranodal site when no nodal involvement is observed or when there is a medical statement that the origin was in an extranodal site, i.e., stomach, skin, lung. (However, nodal and extranodal lymphomas have been grouped together for this monograph.)

2) Histologic type: Differences in histologic type refer to differences in the first 3 digits of morphology as delineated in the ICD-O.

3) Simultaneous: Diagnoses within 2 months of each other are considered to be simultaneous primary cancers.

Rules for Coding Multiple Primary Cancers in Connecticut

1) A single lesion of 1 histologic type is considered a single primary cancer even if the lesion crosses site boundaries.

2) A single lesion with multiple histologic types is considered as a single primary and is coded to the highest histology code number in the absence of an appropriate "mixed histology code," including those given in the rules below.

3) If a new cancer of the same histology as an earlier one is diagnosed in the same site within 2 months, it is considered to be the same primary tumor. If a new cancer of the same histology is diagnosed in the same site after 2 months, this new cancer is considered a separate primary unless stated to be recurrent or metastatic. Exception: Bladder cancer, ICD-O site code 188 with morphology code 8120–8130, is recorded singularly regardless of interval of time.

4) Simultaneous multiple lesions of the same histologic type within the same primary site are considered a single primary cancer. Furthermore, if a lesion has a behavior code of in situ and another a behavior code of malignant, it is considered to be a single primary whose behavior is malignant. Multiple lesions of the same histologic type occurring in different organs are considered to be separate primary tumors unless stated to be metastatic.

5) Multiple lesions of different histologic types within a single organ are considered separate primary cancers whether occurring simultaneously or at different times. Similarly, multiple lesions of different histologic types occurring in different sites are considered separate primary tumors whether occurring simultaneously or at different times. The following are exceptions to this rule:

a) For multiple lesions within a single site occurring within 2 months, if 1 lesion is stated to be (adeno)-carcinoma, NOS, and the second lesion is stated to be a more specific (adeno)carcinoma, it is considered to be a single primary tumor and coded to the more specific (adeno)carcinoma.

b) Within each breast the following combinations of ductal and lobular carcinoma occurring within 2 months of each other are considered a single primary cancer and the histology coded accordingly:
   (1) Infiltrating duct carcinoma (8500/3) and lobular carcinoma (8520/3) are coded to histology 8522/3.
   (2) Infiltrating duct carcinoma (8500/3) and lobular carcinoma-in-situ (8520/2) are coded to histology 8523/3.
   (3) Intraductal carcinoma (8500/2) and lobular carcinoma (8520/3) are coded to histology 8524/3.
   (4) Intraductal carcinoma (8500/2) and lobular carcinoma-in-situ (8520/2) are coded to 8522/2.

   Note that for the female breast, even if the ductal and lobular lesions are reported to occur in different quadrants of the same breast, the appropriate site code is 174.9 (breast, NOS). If the ductal lesions occurs in one breast and the lobular lesion occurs in the opposite breast, these are considered to be 2 primary cancers whether diagnosed within 2 months or not.

c) Within each breast, a combination of Paget's disease with intraductal carcinoma is considered 1 primary cancer.

6) If only 1 histologic type is reported and if both sides of a paired organ are involved within 2 months of diagnosis, a determination must be made as to whether the patient has 1 or 2 independent primary cancers. This determination is generally made by the pathologist based on whether areas of in situ cancer are seen in each side of the paired organ. If it is determined that there are 2 independent primary cancers, 2 records are coded, each with the appropriate laterality. If it is determined that only 1 primary cancer developed, laterality is coded according to the side in which the single primary cancer originated and a single record coded. If it cannot be determined in which side of the paired organ the single primary originated, a single record is coded with laterality not specified. The one exception to this rule is that involvement of both ovaries in which only a single histology is reported is always considered to be a single primary cancer.

HISTORY OF MULTIPLE PRIMARY CANCER STUDIES IN CONNECTICUT

Over the years, investigators have extensively used the resources of the CTR to evaluate the occurrence of multiple primary cancers (*18–32*). The earliest survey was by Greenberg (*18*) in 1959 who reported increased risks for second primary cancers following cancers of the breast or genital organs in females diagnosed between 1935 and 1954. To ensure that metastatic lesions would be excluded, Greenberg required that: 1) The reporting hospital classify the cancer as a second primary, 2) the second cancer occur in a different anatomical site from that of the first cancer, and 3) the interval between the first cancer and the second be at least 5 years. He noted that second cancers of the digestive system and genital organs occurred more frequently than expected after female breast cancer and that second cancers of the digestive system occurred in excess after gynecologic cancers. These results were confirmed when the survey data were updated through 1962 (*19*). Bailar (*20*) also evaluated CTR data to study the risk of nonuterine cancers among patients treated for uterine cancer. His analytic methods were similar to those of Greenberg, although Bailar further restricted the definition of a second primary cancer to sites occurring outside the uterus and to those confirmed by microscopic examination as new and independent neoplasms.

Schoenberg (*21*) prepared a volume of multiple primary cancers in Connecticut, 1935–64, which appears to be the first comprehensive overview and quantitative analysis of the risk of second cancers in patients identified in a well-defined general population. The excess risk of subsequent primary cancer was characterized by organ site, sex, and interval between first and second cancers. Overall, a significant 29% excess of developing a second primary cancer occurred among 120,195 persons.

Several other noteworthy studies of multiple primary cancers in Connecticut have been conducted (*22–32*). Cancers of the breast, corpus uteri, and ovary were found to be associated with colon cancer, and high rates for cancers of the colon, ovary, and prostate were found after rectal cancer (*22*). An excess of breast cancer following meningioma was reported (*23*), as was a bidirectional risk for melanoma and breast cancer (*24*). A significant 40% risk of developing uterine corpus cancer following hormonal treatment for breast cancer was observed for 45,853 breast cancer patients (1935–71) registered by the CTR and 3 hospital-based registries combined (*25*). In an analysis of data collected by the End Results Program, which included the CTR, significant excesses of malignant melanoma, soft tissue sarcomas, and lung cancers were observed among 4,869 patients with CLL (*26*). A study of cervical cancer patients in Connecticut (1935–78) revealed excess second cancers in heavily irradiated organs and a deficit of breast cancer following radiotherapy (*27*). An investigation of 182,040 women treated for cervical cancer and reported to 15 international cancer registries, including the CTR, further quantified the risk of second cancer development following radiation treatment, and for the first time a slight excess of leukemia attributable to intense radiotherapy was reported (*28*). Increased risks for breast cancer following thyroid cancer and thyroid cancer after breast cancer occurred during 1935–78 (*29*). A review of all second cancers following cancer of the salivary gland in 782 patients found an increased risk for respiratory cancers in males and ovarian cancer in females (*30*). An excess risk of leukemia associated with radiotherapy for uterine cancer and chemotherapy for cancers of the breast and ovary and multiple myeloma was reported among 440,000 patients diagnosed during 1973–80 from the SEER Program including the CTR (*31*). Women with breast cancer were also found to be at a threefold risk of developing a second breast cancer in Connecticut (*32*). Thus this monograph on multiple primary cancers is built upon a firm foundation of research conducted during the last 30 years with the use of data from the CTR.

SIMULTANEOUS PRIMARY CANCERS

Simultaneously diagnosed primary cancers are defined as those occurring within 2 months of each other. Although simultaneous tumors are recorded in Connecticut, they have been excluded from all analyses in the monograph chapters but are described here for completeness. Any discrepancies between the number of primary cancers presented in the monograph and the number previously reported from Connecticut are likely the result of our excluding persons with simultaneous cancers, as well as excluding persons who died within 2 months of their initial primary cancer and those for whom the initial primary cancer was diagnosed only on the basis of an autopsy report or a death certificate. Interestingly, the CTR attempts to specify the order of simultaneous primaries by ranking them according to malignant potential or life-threatening impact. For example, breast cancer would be considered the first primary if thyroid cancer were diagnosed simultaneously but would be designated the second if ANLL were the simultaneous diagnosis. The ordering is done randomly when it is not clear which tumor would be considered the most life-threatening.

Over the years 1935–82 in Connecticut, 4,107 persons developed simultaneous cancers. In contrast, 2,286 second cancers occurred between 2 and 12 months after the diagnosis of a first primary cancer versus 1,785 expected (RR = 1.3) had the rates in the general population prevailed. Persons who developed simultaneous tumors accounted for 1.2% of all initial cancers and 19.7% of all second cancers reported in Connecticut (text-table 4). The most frequent simultaneous tumors were cancers of the colon, rectum, prostate, lung, breast, and bladder. Simultaneous primary cancers also were frequently reported for sites in the same organ system or in close proximity to one another such as the colon and rectum, the kidney and bladder, ovary and uterus, prostate and bladder, and prostate and colon.

The number of simultaneous cancers may influence the observed-to-expected ratios occurring over time for some second primary cancers. For example, hematopoietic cancers with long prodromal stages, such as CLL and multiple myeloma, might be diagnosed earlier as a result of the medical work-up for another cancer. These simultaneous cancers would be removed from subsequent analyses, and deficits resulting within 1 or 2 years of follow-up could conceivably be due to the advancement in time of these diagnoses. This artifact of screening appears to have occurred for CLL following certain cancers reported to the SEER Program (*31*) and has been offered as an explanation for a deficit of multiple myeloma seen after cervical cancer (*28*). Similarly, cancers such as the thyroid, cervix, or prostate, which are particularly susceptible to detection during medical surveillance and screening, are frequently diagnosed simultaneously, and the overall pattern of cancer risk over time may be distorted.

The number of simultaneous cancers for each site from text-table 4 was also compared with the total number of

TEXT-TABLE 4.—*Distribution of patients with simultaneous primary cancers among males and females, Connecticut, 1935–82*[a, b]

Cancer site/type	Lip	Tongue	Salivary	Oral	Pharynx	Esophagus	Stomach	Sm intest	Colon	Rectum	Liver	Pancreas	Nasal	Larynx	Lung	Breast	Cervix	Uterus	Ovary	Prostate	Testis	Kidney	Bladder	Melanoma	Eye	Brain	Thyroid	Bone	Connective	NHL	HD	Myeloma	ALL	CLL	ANLL	Other leuk	Other
Lip	5																																				
Tongue	1	3																																			
Salivary	0	0	2																																		
Oral	2	16	0	13																																	
Pharynx	0	6	0	25	5																																
Eosphagus	1	5	0	11	12	1																															
Stomach	1	1	1	1	1	11	4																														
Sm intest	0	0	0	0	1	0	0	2																													
Colon	3	0	1	5	4	2	50	17	545																												
Rectum	3	2	0	3	2	4	14	5	314	70																											
Liver	0	0	0	1	0	3	11	0	21	6	3																										
Pancreas	0	0	0	1	0	1	5	1	15	7	9	0																									
Nasal	1	0	0	2	1	0	0	0	2	0	0	0	0																								
Larynx	1	7	0	13	16	9	2	0	7	3	1	0	0	4																							
Lung	0	5	0	20	7	10	17	5	41	27	12	9	0	30	51																						
Breast	0	2	2	2	2	3	14	2	72	35	12	6	1	2	26	174																					
Cervix	0	0	0	0	1	0	1	0	5	6	1	2	1	0	4	13	4																				
Uterus	0	1	1	0	0	0	2	0	26	9	0	2	0	0	7	46	27	23																			
Ovary	0	0	0	0	0	0	3	2	48	15	2	4	1	0	1	23	4	149	16																		
Prostate	3	2	1	4	1	9	44	2	102	64	18	32	0	9	130	0	0	0	0	3																	
Testis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	6																
Kidney	0	0	0	0	1	3	10	3	23	6	11	3	0	0	16	8	4	3	2	52	0	23															
Bladder	0	0	0	1	1	2	9	0	18	14	2	7	2	3	35	6	6	6	4	254	1	66	13														
Melanoma	0	0	0	1	0	2	1	0	3	3	0	1	0	0	4	6	0	0	0	2	0	0	3	15													
Eye	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	3	0	0	0	1	0	0	0	0	0												
Brain	0	0	1	0	0	0	2	0	4	3	0	1	0	0	3	6	0	2	0	8	1	3	0	0	0	1											
Thyroid	1	0	0	2	1	1	7	0	3	0	2	1	0	2	8	2	0	0	0	5	0	0	0	0	0	3	4										
Bone	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	1	0	0	0	1	0	0	0	1	0	0	0	0									
Connective	1	0	0	0	0	0	2	0	2	0	0	0	0	0	2	0	0	1	0	2	0	3	2	1	1	0	1	0	2								
NHL	0	1	1	0	0	3	6	0	21	8	0	1	1	1	17	11	2	2	0	15	1	2	5	0	0	0	3	0	1	5							
HD	0	0	0	0	0	0	0	1	0	2	1	0	0	1	0	0	0	0	1	1	0	3	3	1	0	0	2	0	0	0	0						
Myeloma	0	0	0	0	1	1	3	0	8	1	1	2	0	0	5	5	1	2	0	5	0	5	1	0	0	0	0	0	0	2	0	0					
ALL	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0				
CLL	1	1	1	3	0	1	5	0	16	2	3	2	0	2	19	5	2	2	1	16	0	3	2	1	0	0	0	0	1	0	0	1	0	0			
ANLL	0	0	0	0	0	0	0	0	1	1	0	0	0	1	2	2	0	1	0	3	0	1	1	0	0	2	1	0	0	0	0	1	0	0	0		
Other leuk	0	0	0	2	1	0	4	0	7	3	1	3	0	2	8	6	1	2	1	12	0	3	2	0	0	0	0	0	0	0	0	4	0	0	0	0	
Other	1	0	0	4	3	6	5	0	13	12	4	1	0	3	14	22	7	19	3	27	3	4	18	1	1	3	4	1	3	2	0	3	0	3	0	3	8
Total[c]	25	53	11	132	92	102	238	41	1401	645	125	116	12	120	535	521	92	333	280	832	15	261	487	46	7	43	53	7	25	111	16	52	4	93	17	65	201

[a] Abbreviations: Oral = oral cavity, Nasal = nasal cavities, Uterus = uterine corpus, Sm Intest = small intestine, Connective = connective tissue, NHL = non-Hodgkin's lymphoma, HD = Hodgkin's disease, Myeloma = multiple myeloma, ALL = acute lymphocytic leukemia, CLL = chronic lymphocytic leukemia, ANLL = acute nonlymphocytic leukemia, Other leuk = other leukemia types, Other = other cancers and unknown primary sites.

[b] A total of 4,107 patients developed 8,124 simultaneous cancers, and 1,005 persons developed simultaneous cancers of the same site. *Numbers in the interior of the table* represent patients with pairs of simultaneous cancers.

[c] Each number in the total row represents the sum of the vertical and horizontal tabulations for that particular cancer site, with the intersection counted once. For example, in the first column, 25 is the number of persons who developed a simultaneous tumor of the lip; however, the total number of simultaneous lip cancers is 30 because 5 persons (the intersection of lip row with lip column) developed a simultaneous tumor of this same site.

nonsimultaneous second primaries for the same site. The number of CLL discovered at the time of the first cancer almost equaled the number of CLL diagnosed during the entire follow-up period of the study (93 vs. 105). The high proportion of simultaneous CLL probably accounts for the decreased risk of CLL seen during the first 5 years following the diagnosis of most first cancers. A high ratio (79%) of simultaneous to nonsimultaneous multiple primary cancers of the testis (15 vs. 19) was also observed. Cancers for which the ratio of simultaneous to nonsimultaneous cancer was 50% or greater included the gum and other mouth, pharynx, small intestine, colon, rectum, liver, larynx, cervix uteri, ovary, prostate, testis, kidney, bladder, thyroid, and CLL. The smallest ratio was for ANLL (9%), and ratios less than 25% were found for cancers of the salivary gland, breast, bladder, bone, and connective tissue.

SUBJECTS AND METHODS FOR ANALYSIS OF MULTIPLE PRIMARY CANCERS

Patients selected for the current analysis of multiple primary cancers were Connecticut residents at the time of diagnosis of their first primary invasive cancer. Neoplasms with behavior designated as benign, uncertain malignancy, or in situ, and basal or squamous cell skin cancers were excluded. There were 330,371 patients meeting these criteria who were diagnosed with their first cancer during January 1, 1935 to December 31, 1982. A total of 76,835 patients (23.3%) were excluded from the analysis for the following reasons: The initial cancer was identified solely on the basis of a death certificate or an autopsy report (31,796); survival or the period of observation after the first cancer diagnosis was less than 2 months (40,932); or the second cancer occurred less than 2 months from the first cancer (4,107), i.e., could be classified as a simultaneous cancer. The total number of patients included in the study was thus 253,536, of whom 16,727 (6.6%) developed a second nonsimultaneous primary cancer.

Second primary cancers were defined as all invasive tumors that developed at least 2 months after the diagnosis of the first cancer. In situ cancers and all nonmelanoma skin cancers were excluded, as were any third and fourth primary cancers. Site and histology for first and second cancers were coded according to the ICD-O (*15*). The percent of first and second cancers that were microscopically confirmed is indicated for each cancer site in the monograph tables. Second cancers identified only by death certificates or autopsy reports were included in all analyses.

The proportion of patients who received radiotherapy as part of their first course of treatment is presented in the monograph tables for each cancer site. Documentation for radiotherapy as well as surgery is usually available because it is most often administered in the hospital. Chemotherapy, however, tends to be underreported in the Registry records because it is frequently initiated directly from a physician's office and thus not necessarily recorded in hospital records. We chose not to tabulate the proportion of cancer patients known to have received chemotherapy because the potential for incomplete ascertainment in Registry records could not be assessed.

The CTR records the first course of cancer-directed therapy, i.e., any therapy given during the first 4 months after initiation of treatment, regardless of the interval between diagnosis and first treatment. Treatment for leukemia is recorded for the first 2 months following initiation of therapy only. More than 1 treatment modality is recorded if used during the first course. Data on therapy given subsequent to the first course of treatment are not generally available in the Registry records. If a new therapy is initiated due to failure of the previous treatment or progression of disease, it is considered a second course and is not included in the CTR record. In addition, palliative therapy to alleviate symptoms only is not recorded by the Registry.

Patients were considered at risk for a second primary cancer during the period beginning 2 months from the date of diagnosis of the first primary cancer. For persons in whom no second cancer developed, the end of the period of risk was taken as the date of last contact, i.e., the date of death for those who died, the date last known alive, or December 31, 1982, whichever occurred first. For persons who developed a second cancer, the end of the period of risk was the date the second cancer was diagnosed. The total number of second cancers was tabulated for each site and for each period. We applied 5-year age, 5-year calendar period, and sex-specific incidence rates for each cancer to the appropriate person-years under observation to obtain the numbers of second primary cancers expected had these patients experienced the same rates as prevailed in the corresponding Connecticut population (*33*).

The statistical methods used were based on the assumption that the observed number of second cancers in any specific category will follow a Poisson distribution. Tests of significance and 95% confidence interval for the RR, taken as the ratio of observed-to-expected incident cancers, were calculated with the use of an accurate asymptotic approximation to the Poisson distribution (*34*). Testing for linear trend of increasing RR with increasing time since primary cancer diagnosis was done according to the method of Breslow et al. (*35*).

CAUTIONS IN INTERPRETATION

The results from our analyses of multiple primary cancer must be interpreted in light of changes in medical care and reporting practices that occurred over the many years of cancer registration in Connecticut (*36*). Risk factors common to multiple cancer have also varied over time, as illustrated by the increasing proportion of smokers among women in our population (*6*). Intense medical surveillance and conditions peculiar to the evaluation of second cancers (e.g., misclassified metastases and autopsy diagnoses) may also affect the reported incidence of second cancers. The practice of radiation therapy changed as supervoltage machines replaced orthovoltage units, and different dose distributions to distant organs may alter the pattern of second cancer occurrence. New therapies, such as chemotherapy, have been introduced, which have affected the risk of some second cancers, most notably ANLL (*31*). Some findings might be influenced by changes in coding classifications and by misclassifications of therapy in Registry records. The special advantages of this survey, however, are the exceptionally large number of subjects studied in a population-based cancer registry, the long follow-up available (almost 50 yr), and the strict criteria used by a single registry to record second primary cancers. Thus our study of multiple primary cancers in Connecticut provides investigators with a special opportunity to estimate risks and clarify constellations of multiple cancer, to generate and evaluate etiologic hypotheses, and to provide strategy for more definitive research into the origins of cancer and means of prevention.

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Second Cancer Following Cancers of the Buccal Cavity and Pharynx in Connecticut, 1935–1982 [1]

Deborah M. Winn *and* William J. Blot [2]

ABSTRACT—Patients diagnosed in Connecticut from 1935 to 1982 with cancers of the tongue, gum, floor, and other parts of the mouth, or pharynx experienced twofold to threefold increased risks of developing a second primary cancer. The excesses were most prominent [relative risk (RR) ≥ 10] for subsequent oral and esophageal cancers but also were observed for cancers at other sites in the digestive and respiratory tracts. The increased risks, which affected both men and women and persisted over time, are most likely related to increased alcohol and tobacco consumption in the patients developing second primaries. The proportion of persons developing a new primary was 9% among the 2,120 patients with cancer of the tongue, 14% for the 3,063 patients with cancer in the gum, floor, or other parts of the mouth, and 8% among the 2,637 persons with pharynx cancer. If one considers that the average length of follow-up was only 3.4 years, these percentages are high and indicate the need for continued surveillance of patients with oral and pharyngeal cancers. Small overall excesses of subsequent cancer occurred among patients with initial lip (RR = 1.3) or salivary gland cancers (RR = 1.2), with twofold risks of oral and respiratory cancers evident for both tumors.—Natl Cancer Inst Monogr 68: 25-48, 1985.

LIP CANCER (ICD-O, 140)

Cancers of the lip are rare and account for about 0.6% of all cancers in the United States (*1*). The tumors occur almost exclusively in white males. Prognosis is often excellent, as the estimated 5-year relative survival rate is 85% (*2*). It has long been established that actinic (UV) radiation is a risk factor and that men with outdoor employment (e.g., farming) and long exposure to sunlight are most susceptible. However, lip cancer does not share with skin cancer the same sharp gradient of incidence with latitude (*3*). Also implicated in lip cancer causation is the smoking of pipes, cigars, and cigarettes (*4*).

Results

In Connecticut, 1,972 persons were diagnosed with lip cancer between 1935 and 1982. Here, as elsewhere in the United States, the overwhelming proportion of patients (92%) were men. The average age at onset of lip cancer was 64 years.

During the 9-year average period of follow-up after an initial cancer of the lip, 347 (333 among males, 14 among females) subsequent primary cancers were diagnosed, compared with 270 expected based on general population rates (RR = 1.29; 95% CI = 1.2–1.4). The excess was primarily limited to cancers of the respiratory tract (RR = 1.8; 95% CI = 1.4–2.3) and buccal cavity and pharynx (RR = 3.4; 95% CI = 2.5–4.6). The increased risks for oral cancers among men were observed for all subsites, including the lip, tongue, salivary gland, gum, floor of the mouth, and pharynx.

Because few women in Connecticut developed lip cancer, the remainder of this section involves men only. When examined by time since diagnosis, men with lip cancer continued to experience an excess of subsequent cancer even after 10 years of follow-up. However, a downward trend was apparent in the risk of subsequent cancer of the buccal cavity and pharynx, as the RR declined from 5.5 to 2.2 over time. This trend was most striking for new primaries arising from the lip, with RR ranging from 7.4 shortly after diagnosis to 2.9 among persons followed for 10 and more years.

Excess risks for cancer sites throughout the respiratory system were observed in males with lip cancer. Laryngeal cancer risks were highest (RR = 2.5; 95% CI = 1.3–4.2), followed by lung cancer (1.7; 95% CI = 1.4–2.2). The excesses of laryngeal and lung cancers occurred throughout all follow-up intervals, except for a slight deficit of lung cancer in the early postdiagnosis period. No significant excess was observed for second cancers of the digestive or other systems, except for leukemia ($n = 14$; RR = 1.8; 95% CI = 1.0–3.0), which was also significantly elevated in women. Rates of melanoma were not elevated (2 observed vs. 2.1 expected).

Discussion

Patients with lip cancer in this survey were more likely to develop a second lip cancer, and cancers elsewhere in the oral cavity, pharynx, larynx, and lung than were persons in the Connecticut general population. These findings are consistent with other investigations (*5–7*). It seems likely that tobacco smoking is a major risk factor underlying this pattern of multiple primary cancers. Malignant melanoma (the only skin cancer for which data were available) was not more common in the patients with lip cancer, although skin cancer has been shown to occur

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ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Biostatistics Branch, Division of Cancer Etiology, Landow Building, Room 3C16, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Deborah M. Winn, Ph.D.

excessively in patients with lip cancer (*6–8*), probably due to increased sunlight exposure. The twofold increase of leukemia subsequent to lip cancer is noteworthy, but reasons for this association are not clear.

SALIVARY GLANDS (ICD-O, 142)

Cancers of the salivary gland are rare, accounting for about 0.3% of cancer cases and 0.1% of all cancer deaths in the United States (*1*). The cancers are usually treated by surgery only (61%) or by radiation with or without surgery (36%), usually with success. The 5-year relative survival rates have been estimated to be 64% for males and 78% for females (*2*). The causes of salivary gland cancers, which occur slightly more often among men than women, are obscure, except that some cases have been linked to high doses of ionizing radiation (*9*).

In earlier surveys of second primary tumors following salivary gland cancer in which data from the Connecticut Tumor Registry were used, no increased incidence of cancer was detected in 1935–64 (*10*), but for the period 1935–78 the risk of all cancers combined was increased (1.4), with the excess mainly for respiratory cancer in males, RR = 2.8, and ovarian cancer in females, RR = 5.3 (*11*).

Results

Of the 855 persons (444 males, 411 females) who developed salivary gland cancer in Connecticut during 1935–82 and who were followed for an average of 7.4 years, 65 (32 males, 33 females) developed second primary cancers, compared with 55 expected based on rates in the general population (RR = 1.2; 95% CI = 0.9–1.5). Most of the excess risk was accounted for by respiratory cancers ($n = 16$; RR = 2.2; 95% CI = 1.3–3.6), with some nonsignificant increases of oral cancer (RR = 2.6; 95% CI = 0.8–6.1) and ovarian cancer (RR = 3.3; 95% CI = 0.9–8.5). Three of the 5 cancers of the buccal cavity arose on the lip. The oral and respiratory cancers occurred primarily among males and persisted among those followed 5–9 years and 10 or more years, as did the excess of ovarian cancer among females. The increased rates of respiratory and ovarian cancers were detected in patients with and without radiotherapy for salivary gland cancer, but the relative excesses were more pronounced in the radiation-treated group. Eight women had diagnoses of breast cancer, compared with 7.1 expected.

Discussion

A slight increase in second cancers occurred among persons with salivary gland cancer. The increased risk was largely due to cancers of the respiratory tract, especially the lung but also the larynx, and was seen mainly among males. The association with lung cancer is bidirectional, inasmuch as lung cancer patients in Connecticut were at increased risk of salivary gland cancer (*12*). The association was seen even among long-term survivors, which suggests that salivary and respiratory cancers may share etiologic factors, although tobacco smoking is not known to cause salivary gland cancer (*13*). Radiation exposure from therapy to the salivary glands may reach the larynx and lungs but at doses thought to be low. Because radiation is known to increase the risk of lung cancer (*14*), however, a small part of the excess may be radiation related. An increased risk of lung cancer was also observed in a British series of patients with salivary gland cancer (*15*). The excess of buccal cavity cancer, mostly of the lip, may be partly due to increased medical surveillance. The increase of ovarian cancer may be due to chance because multiple comparisons were made, and the increases in risks were not statistically significant. No clear association was found with breast cancer. This observation is contrary to some reports of an association (*15–17*), although it is consistent with a study suggesting no relationship between cancers of the salivary gland and breast (*11*).

ORAL CAVITY AND PHARYNX (ICD-O, 141, 143–149)

Cancers of the oral cavity and pharynx are divided into 3 categories for analysis: the tongue; the gum, floor of mouth, and other parts of the mouth; and the pharynx. These tumors, mostly squamous cell in origin, represent 0.6, 0.9, and 1.0%, respectively, of all cancers (*1*). They occur predominantly among males and are strongly associated with alcohol consumption and the use of tobacco in any form, including cigarettes, pipes, cigars, chewing tobacco, and snuff (*3, 18*).

However, some dissimilarities among anatomic sites exist within the mouth and throat. Pharynx cancer has a poorer prognosis, with 5-year survival rates for whites of 23%, whereas the survival rates for tongue and gum/floor of mouth are 36 and 43%, respectively (*1*). Although intersite differences in etiology are not well understood, particular anatomic areas may be more influenced by tobacco and alcohol (*19*). For example, cancers of the gum and buccal mucosa are more strongly associated with snuff dipping than cancers of other oral or pharyngeal sites (*20*). Risk factors for cancers of the nasopharynx differ from those for cancers occurring in the rest of the oral cavity and pharynx (*21*), but nasopharyngeal cancers were combined with pharyngeal cancers in our analyses because of their rarity, i.e., only 18 second primary cancers developed in 445 persons with cancer of the nasopharynx.

The risk of multiple primaries is known to be high among patients with cancers of the oral cavity and pharynx, with tumors mainly affecting the same anatomic region, plus the esophagus, larynx, and lung (*5, 6, 22*). Smoking and alcohol use prior to the onset of the initial cancer are thought to enhance the risk of these second primaries (*7, 23, 24*), but it is not entirely clear whether the risk is lowered if these habits are discontinued after diagnosis of the first neoplasm (*25, 26*).

Results

In Connecticut over the 1935–82 study period, 7,820 persons developed an oral or pharyngeal cancer. The age at cancer onset was similar for patients with cancers of the various subsites, averaging 62 years for males and 61 for females. Follow-up was shortest and the percent of cases with a second cancer was the smallest for patients with cancer of the pharynx, the site with the least favorable prognosis.

Patients with oral and pharyngeal cancer experienced an increased risk of second cancer. A total of 198 (or 9%) new primaries developed in 2,120 patients with tongue cancer; 424 (or 14%) in the 3,063 patients with cancer of the gum, floor of mouth, or other parts of the mouth; and 208 (or 8%) in the 2,637 patients with pharynx cancer. All observed numbers were higher than expected based on general population rates. The RR (and 95% CI) were similar for each group: 2.3 (2.0–2.7), 2.7 (2.5–3.0), and 2.5 (2.2–2.9), respectively. The risk of new primaries was especially high ($\geq$ 10) in the buccal cavity, pharynx, and esophagus. The increased risk was seen for all subsites in the oral cavity and pharynx and occurred among both sexes, although the relative excesses tended to be higher among women. The trend in risk was downward over time, but sizable increases still persisted even after 10 or more years had elapsed since the diagnosis of the first primary neoplasm.

A significant increase in prostate cancer was also seen (RR = 1.7; 95% CI = 1.3–2.1), and it persisted over time. Three female patients developed cervical cancer, compared with 2.1 expected based on general population rates.

Radiation therapy was a common initial treatment for patients with cancer of the tongue (63.3%), gum, floor or other parts of the mouth (56.2%), and pharynx (85.4%), but the risks of second cancer for those with or without radiation treatment were generally similar.

Significant increases of subsequent respiratory and digestive (other than esophageal) tract cancers also were observed. The excess of respiratory cancer affected cancers of the nasal passages (RR = 7.5), larynx (RR = 5.0), and lung (RR = 3.1) The excess of digestive cancers affected cancers of the stomach (RR = 1.8), colon (RR = 1.6), liver and biliary tract (RR = 2.3), and pancreas (RR = 1.7), but not the rectum (RR = 1.0). The increased risk of respiratory cancer persisted over time, but only a slight excess of digestive cancer (excluding the esophagus) was observed 10 or more years after the diagnosis of oral and pharynx cancer.

Discussion

A high risk of second tumors after an initial cancer of the oral cavity and pharynx is clearly evident in the data from the Connecticut Tumor Registry. Although follow-up averaged only 3.4 years, 8 to 14% of the patients developed a new primary neoplasm. These percentages are exceptionally high and can only increase as follow-up is extended. A previous survey of 377 patients with cancers of the floor of the mouth revealed that 27% developed new primaries at other sites over an 18-year accrual and follow-up period (*22*). Because of their high risk of additional cancers, patients with oral and pharyngeal cancer should remain under continued medical surveillance.

The increased risk of subsequent cancer extended to several sites in the oral cavity and pharynx as well as in the digestive and respiratory systems; the risk was evident long after the initial cancer diagnosis. The incidence of new oral and esophageal cancers was striking, with relative excesses exceeding tenfold. Not only are patients with oral and pharyngeal cancer at high risk of esophageal cancer, but an exceptional risk of oral and pharyngeal cancer is seen after esophageal cancer in Connecticut (*27*). The same bidirectional association holds for oral and laryngeal cancers (*12*). Inasmuch as alcohol and smoking are the primary determinants of these cancers, they seem likely to account for much of the increased risk of subsequent cancer among patients with oral and pharyngeal cancer. The higher relative risks in women than men also may be related to smoking and drinking habits. Although both male and female patients with oral cancer typically have high intakes of alcohol and tobacco, the relative increase in intake may have been greater for women with oral cancer because of their lower base-line consumption levels.

That patients with oral and pharyngeal cancer have an increased risk of subsequent cancer in the same anatomic region is well documented (*5, 10, 22, 28, 29*). The association of oral cancer with esophageal and respiratory cancers has also been described (*5, 10, 22, 30*). However, the small but consistent elevation in risks we observed for most digestive tract sites, except the rectum, have not previously been reported and deserve further study. The association with some cancers (e.g., pancreas, liver) may be related to tobacco smoking or alcohol intake. The association with colon cancer may be related to alcohol consumption, although the effects on the large bowel reported for beer drinking have mainly involved rectal cancer (*31*). The excess of prostate cancer appears due to the increased diagnostic scrutiny of cancer patients. Some previous studies have suggested that oral and cervical cancers occur excessively together (*32, 33*), but this association was not seen in this survey, although the numbers involved are small.

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LIP
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the lip, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,819	153	1,972
No. who developed a second primary cancer	333	14	347
Average age at diagnosis of first cancer, yr	64	66	64
Average yr of diagnosis of first cancer	1956	1961	1957
Person-yr of follow-up	16,720	1,103	17,823
Average follow-up, yr	9.2	7.2	9.0
Percent given radiotherapy for first cancer	24.4	28.8	24.7

[a] ICD-O code = 140.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the lip in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	268	77.2
Only the first cancer	55	15.9
Only the second cancer	15	4.3
Neither first nor second cancer	9	2.6
Total second primary cancers	347	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LIP
BOTH SEXES

TABLE 1C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the lip among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,972			1,813			1,182			721			1,972		
Person-yr in interval	1,573			5,820			4,660			5,771			17,823		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**23**	**19.41**	**1.2**	**106**	**75.22**	**1.4**[b]	**88**	**67.82**	**1.3**[b]	**130**	**107.49**	**1.2**[b]	**347**	**269.80**	**1.3**[b]
All excluding site of initial cancer	**21**	**19.14**	**1.1**	**99**	**74.26**	**1.3**[b]	**85**	**67.01**	**1.3**[b]	**127**	**106.46**	**1.2**	**332**	**266.72**	**1.2**[b]
Buccal cavity, pharynx	**6**	**1.10**	**5.4**[b]	**17**	**4.11**	**4.1**[b]	**13**	**3.55**	**3.7**[b]	**11**	**4.97**	**2.2**[b]	**47**	**13.72**	**3.4**[b]
Lip	2	0.27	7.3	7	0.96	7.3[b]	3	0.81	3.7	3	1.03	2.9	15	3.08	4.9[b]
Tongue	1	0.22	4.6	4	0.81	4.9[b]	6	0.69	8.7[b]	3	0.95	3.2	14	2.67	5.3[b]
Salivary gland	0	0.05	0.0	0	0.20	0.0	1	0.18	5.6	2	0.29	6.9	3	0.72	4.2
Gum, other mouth	1	0.29	3.5	5	1.08	4.6[b]	1	0.94	1.1	2	1.35	1.5	9	3.65	2.5[b]
Pharynx	2	0.23	8.8	1	0.88	1.1	2	0.79	2.5	1	1.16	0.9	6	3.06	2.0
Digestive system	**4**	**6.97**	**0.6**	**23**	**26.64**	**0.9**	**25**	**23.51**	**1.1**	**39**	**35.14**	**1.1**	**91**	**92.21**	**1.0**
Esophagus	1	0.46	2.2	3	1.79	1.7	2	1.57	1.3	4	2.12	1.9	10	5.94	1.7
Stomach	0	1.62	0.0	8	5.95	1.3	3	4.99	0.6	7	6.59	1.1	18	19.13	0.9
Colon	3	2.35	1.3	2	9.18	0.2[b]	9	8.32	1.1	21	13.41	1.6	35	33.24	1.1
Rectum	0	1.39	0.0	6	5.31	1.1	6	4.71	1.3	6	7.03	0.9	18	18.43	1.0
Liver, biliary	0	0.36	0.0	1	1.36	0.7	0	1.19	0.0	0	1.82	0.0	1	4.73	0.2
Pancreas	0	0.67	0.0	3	2.57	1.2	4	2.32	1.7	1	3.59	0.3	8	9.15	0.9
Respiratory system	**3**	**2.97**	**1.0**	**25**	**11.94**	**2.1**[b]	**20**	**11.13**	**1.8**[b]	**33**	**18.61**	**1.8**[b]	**81**	**44.63**	**1.8**[b]
Nasal cavities, sinuses	0	0.05	0.0	1	0.17	5.8	0	0.15	0.0	0	0.23	0.0	1	0.60	1.7
Larynx	1	0.39	2.6	3	1.52	2.0	5	1.36	3.7[b]	4	1.98	2.0	13	5.25	2.5[b]
Trachea, bronchus, lung	2	2.50	0.8	21	10.14	2.1[b]	15	9.53	1.6	29	16.26	1.8[b]	67	38.41	1.7[b]
Female breast	1	0.30	3.4	0	1.09	0.0	0	0.75	0.0	0	0.71	0.0	1	2.85	0.4
Female genital tract	**0**	**0.19**	**0.0**	**0**	**0.70**	**0.0**	**1**	**0.45**	**2.2**	**1**	**0.40**	**2.5**	**2**	**1.74**	**1.2**
Cervix uteri	0	0.04	0.0	0	0.14	0.0	0	0.09	0.0	0	0.06	0.0	0	0.33	0.0
Corpus uteri	0	0.07	0.0	0	0.24	0.0	1	0.16	6.4	0	0.16	0.0	1	0.63	1.6
Uterus, NOS	0	0.02	0.0	0	0.08	0.0	0	0.05	0.0	1	0.03	34.7	1	0.18	5.4
Ovary, fallopian tubes	0	0.05	0.0	0	0.18	0.0	0	0.12	0.0	0	0.11	0.0	0	0.46	0.0
Prostate gland	5	3.41	1.5	17	13.30	1.3	9	12.63	0.7	23	22.23	1.0	54	51.54	1.0
Testis	0	0.03	0.0	0	0.12	0.0	1	0.09	11.4	0	0.10	0.0	1	0.34	3.0
Kidney, renal pelvis, ureter	0	0.42	0.0	2	1.67	1.2	0	1.51	0.0	2	2.42	0.8	4	6.02	0.7
Bladder, other urinary	1	1.27	0.8	7	4.98	1.4	5	4.61	1.1	5	7.82	0.6	18	18.67	1.0
Melanoma of the skin	0	0.16	0.0	1	0.61	1.6	0	0.54	0.0	1	0.91	1.1	2	2.20	0.9
Eye	0	0.03	0.0	0	0.11	0.0	0	0.10	0.0	0	0.14	0.0	0	0.38	0.0
Brain, central nervous system	0	0.16	0.0	1	0.61	1.6	2	0.53	3.8	1	0.78	1.3	4	2.08	1.9
Thyroid gland	1	0.05	19.2	0	0.21	0.0	0	0.17	0.0	0	0.24	0.0	1	0.68	1.5
Bone	0	0.04	0.0	0	0.15	0.0	0	0.12	0.0	0	0.13	0.0	0	0.44	0.0
Connective tissue	0	0.10	0.0	1	0.38	2.6	0	0.34	0.0	0	0.52	0.0	1	1.34	0.7
Lymphatic, hematopoietic system	**1**	**1.17**	**0.9**	**7**	**4.62**	**1.5**	**6**	**4.22**	**1.4**	**8**	**6.97**	**1.1**	**22**	**16.98**	**1.3**
Non-Hodgkin's lymphoma	1	0.36	2.8	1	1.41	0.7	0	1.28	0.0	2	2.09	1.0	4	5.13	0.8
Hodgkin's disease	0	0.09	0.0	0	0.35	0.0	0	0.30	0.0	1	0.42	2.4	1	1.17	0.9
Multiple myeloma	0	0.16	0.0	0	0.64	0.0	0	0.60	0.0	0	1.07	0.0	0	2.47	0.0
Leukemias	0	0.56	0.0	6	2.21	2.7	6	2.04	2.9[b]	5	3.39	1.5	17	8.21	2.1[b]
Chronic lymphocytic	0	0.17	0.0	0	0.67	0.0	2	0.64	3.1	1	1.12	0.9	3	2.60	1.2
Acute nonlymphocytic	0	0.13	0.0	2	0.55	3.7	2	0.52	3.9	1	0.95	1.1	5	2.15	2.3

[a] ICD-O code = 140.

[b] $P < .05$.

LIP
MALES

Table 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the lip among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,819			1,669			1,105			681			1,819		
Person-yr in interval	1,450			5,380			4,370			5,520			16,720		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**22**	**18.17**	**1.2**	**103**	**70.59**	**1.5**[b]	**82**	**64.66**	**1.3**[b]	**126**	**104.61**	**1.2**[b]	**333**	**257.91**	**1.3**[b]
All excluding site of initial cancer	**20**	**17.90**	**1.1**	**96**	**69.64**	**1.4**[b]	**79**	**63.85**	**1.2**	**123**	**103.58**	**1.2**	**318**	**254.85**	**1.2**[b]
Buccal cavity, pharynx	**6**	**1.09**	**5.5**[b]	**16**	**4.03**	**4.0**[b]	**13**	**3.50**	**3.7**[b]	**11**	**4.92**	**2.2**[b]	**46**	**13.52**	**3.4**[b]
Lip	2	0.27	7.4	7	0.95	7.3[b]	3	0.81	3.7	3	1.03	2.9	15	3.06	4.9[b]
Tongue	1	0.21	4.7	4	0.80	5.0[b]	6	0.68	8.8[b]	3	0.94	3.2	14	2.63	5.3[b]
Salivary gland	0	0.05	0.0	0	0.19	0.0	1	0.17	5.8	2	0.28	7.1	3	0.69	4.3
Gum, other mouth	1	0.28	3.5	4	1.05	3.8[b]	1	0.92	1.1	2	1.33	1.5	8	3.58	2.2
Pharynx	2	0.22	8.9[b]	1	0.87	1.2	2	0.78	2.6	1	1.15	0.9	6	3.02	2.0
Digestive system	**4**	**6.53**	**0.6**	**23**	**24.99**	**0.9**	**22**	**22.37**	**1.0**	**38**	**34.17**	**1.1**	**87**	**88.01**	**1.0**
Esophagus	1	0.46	2.2	3	1.75	1.7	1	1.55	0.6	4	2.10	1.9	9	5.85	1.5
Stomach	0	1.54	0.0	8	5.68	1.4	3	4.80	0.6	7	6.45	1.1	18	18.47	1.0
Colon	3	2.15	1.4	2	8.43	0.2[b]	8	7.80	1.0	21	12.96	1.6[b]	34	31.33	1.1
Rectum	0	1.31	0.0	6	5.02	1.2	6	4.51	1.3	5	6.86	0.7	17	17.69	1.0
Liver, biliary	0	0.33	0.0	1	1.23	0.8	0	1.10	0.0	0	1.76	0.0	1	4.42	0.2
Pancreas	0	0.62	0.0	3	2.42	1.2	4	2.21	1.8	1	3.49	0.3	8	8.74	0.9
Respiratory system	**3**	**2.91**	**1.0**	**24**	**11.72**	**2.0**[b]	**20**	**10.99**	**1.8**[b]	**32**	**18.44**	**1.7**[b]	**79**	**44.03**	**1.8**[b]
Nasal cavities, sinuses	0	0.04	0.0	1	0.17	6.1	0	0.15	0.0	0	0.22	0.0	1	0.58	1.7
Larynx	1	0.39	2.6	3	1.51	2.0	5	1.35	3.7[b]	4	1.97	2.0	13	5.22	2.5[b]
Trachea, bronchus, lung	2	2.45	0.8	20	9.94	2.0[b]	15	9.40	1.6	28	16.10	1.7[b]	65	37.88	1.7[b]
Prostate gland	5	3.41	1.5	17	13.30	1.3	9	12.63	0.7	23	22.23	1.0	54	51.54	1.0
Testis	0	0.03	0.0	0	0.12	0.0	1	0.09	11.4	0	0.10	0.0	1	0.34	3.0
Kidney, renal pelvis, ureter	0	0.40	0.0	2	1.60	1.3	0	1.47	0.0	2	2.37	0.8	4	5.83	0.7
Bladder, other urinary	1	1.23	0.8	7	4.83	1.4	5	4.51	1.1	5	7.73	0.6	18	18.30	1.0
Melanoma of the skin	0	0.14	0.0	1	0.56	1.8	0	0.51	0.0	1	0.87	1.1	2	2.09	1.0
Eye	0	0.03	0.0	0	0.11	0.0	0	0.09	0.0	0	0.13	0.0	0	0.36	0.0
Brain, central nervous system	0	0.15	0.0	1	0.58	1.7	1	0.51	2.0	1	0.75	1.3	3	1.99	1.5
Thyroid gland	1	0.04	22.7	0	0.18	0.0	0	0.15	0.0	0	0.23	0.0	1	0.60	1.7
Bone	0	0.04	0.0	0	0.14	0.0	0	0.11	0.0	0	0.13	0.0	0	0.42	0.0
Connective tissue	0	0.09	0.0	1	0.36	2.8	0	0.32	0.0	0	0.51	0.0	1	1.29	0.8
Lymphatic, hematopoietic system	**1**	**1.10**	**0.9**	**6**	**4.33**	**1.4**	**5**	**4.03**	**1.2**	**7**	**6.78**	**1.0**	**19**	**16.23**	**1.2**
Non-Hodgkin's lymphoma	1	0.33	3.0	1	1.31	0.8	0	1.21	0.0	2	2.02	1.0	4	4.87	0.8
Hodgkin's disease	0	0.09	0.0	0	0.34	0.0	0	0.29	0.0	1	0.41	2.5	1	1.12	0.9
Multiple myeloma	0	0.15	0.0	0	0.59	0.0	0	0.57	0.0	0	1.04	0.0	0	2.35	0.0
Leukemias	0	0.53	0.0	5	2.09	2.4	5	1.96	2.5	4	3.32	1.2	14	7.90	1.8
Chronic lymphocytic	0	0.16	0.0	0	0.63	0.0	1	0.62	1.6	1	1.10	0.9	2	2.51	0.8
Acute nonlymphocytic	0	0.13	0.0	2	0.51	3.9	2	0.49	4.1	1	0.93	1.1	5	2.05	2.4

[a] ICD-O code = 140.

[b] $P < .05$.

LIP
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the lip among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	153			144			77			40			153		
Person-yr in interval	123			440			289			251			1,103		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1**	**1.24**	**0.8**	**3**	**4.63**	**0.6**	**6**	**3.16**	**1.9**	**4**	**2.87**	**1.4**	**14**	**11.89**	**1.2**
All excluding site of initial cancer	**1**	**1.24**	**0.8**	**3**	**4.62**	**0.6**	**6**	**3.16**	**1.9**	**4**	**2.87**	**1.4**	**14**	**11.87**	**1.2**
Buccal cavity, pharynx	**0**	**0.02**	**0.0**	**1**	**0.07**	**13.4**	**0**	**0.05**	**0.0**	**0**	**0.05**	**0.0**	**1**	**0.20**	**5.1**
Lip	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Tongue	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Salivary gland	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Gum, other mouth	0	0.01	0.0	1	0.03	38.2	0	0.02	0.0	0	0.02	0.0	1	0.07	14.5
Pharynx	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Digestive system	**0**	**0.44**	**0.0**	**0**	**1.65**	**0.0**	**3**	**1.15**	**2.6**	**1**	**0.97**	**1.0**	**4**	**4.21**	**1.0**
Esophagus	0	0.01	0.0	0	0.04	0.0	1	0.02	40.8	0	0.02	0.0	1	0.09	10.9
Stomach	0	0.07	0.0	0	0.27	0.0	0	0.19	0.0	0	0.14	0.0	0	0.66	0.0
Colon	0	0.20	0.0	0	0.74	0.0	1	0.52	1.9	0	0.45	0.0	1	1.91	0.5
Rectum	0	0.08	0.0	0	0.29	0.0	0	0.20	0.0	1	0.17	5.7	1	0.74	1.3
Liver, biliary	0	0.03	0.0	0	0.12	0.0	0	0.08	0.0	0	0.07	0.0	0	0.31	0.0
Pancreas	0	0.04	0.0	0	0.16	0.0	0	0.11	0.0	0	0.10	0.0	0	0.41	0.0
Respiratory system	**0**	**0.06**	**0.0**	**1**	**0.22**	**4.6**	**0**	**0.14**	**0.0**	**1**	**0.17**	**5.7**	**2**	**0.59**	**3.4**
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Larynx	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Trachea, bronchus, lung	0	0.05	0.0	1	0.19	5.2	0	0.13	0.0	1	0.16	6.3	2	0.53	3.8
Female breast	1	0.30	3.4	0	1.09	0.0	0	0.75	0.0	0	0.71	0.0	1	2.85	0.4
Female genital tract	**0**	**0.19**	**0.0**	**0**	**0.70**	**0.0**	**1**	**0.45**	**2.2**	**1**	**0.40**	**2.5**	**2**	**1.74**	**1.2**
Cervix uteri	0	0.04	0.0	0	0.14	0.0	0	0.09	0.0	0	0.06	0.0	0	0.33	0.0
Corpus uteri	0	0.07	0.0	0	0.24	0.0	1	0.16	6.4	0	0.16	0.0	1	0.63	1.6
Uterus, NOS	0	0.02	0.0	0	0.08	0.0	0	0.05	0.0	1	0.03	34.7	1	0.18	5.4
Ovary, fallopian tubes	0	0.05	0.0	0	0.18	0.0	0	0.12	0.0	0	0.11	0.0	0	0.46	0.0
Kidney, renal pelvis, ureter	0	0.02	0.0	0	0.07	0.0	0	0.05	0.0	0	0.05	0.0	0	0.18	0.0
Bladder, other urinary	0	0.04	0.0	0	0.15	0.0	0	0.10	0.0	0	0.09	0.0	0	0.38	0.0
Melanoma of the skin	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0
Brain, central nervous system	0	0.01	0.0	0	0.03	0.0	1	0.02	46.8	0	0.02	0.0	1	0.09	11.7
Thyroid gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Bone	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.02	0.0
Connective tissue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Lymphatic, hematopoietic system	**0**	**0.08**	**0.0**	**1**	**0.29**	**3.4**	**1**	**0.19**	**5.1**	**1**	**0.19**	**5.3**	**3**	**0.75**	**4.0**
Non-Hodgkin's lymphoma	0	0.03	0.0	0	0.10	0.0	0	0.07	0.0	0	0.07	0.0	0	0.27	0.0
Hodgkin's disease	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Multiple myeloma	0	0.01	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Leukemias	0	0.03	0.0	1	0.12	8.3	1	0.08	12.2	1	0.07	13.4	3	0.31	9.7[b]
Chronic lymphocytic	0	0.01	0.0	0	0.03	0.0	1	0.02	44.7	0	0.02	0.0	1	0.09	11.5
Acute nonlymphocytic	0	0.01	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0

[a] ICD-O code = 140.

[b] $P < .05$.

TONGUE
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the tongue, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,643	477	2,120
No. who developed a second primary cancer	144	54	198
Average age at diagnosis of first cancer, yr	62	62	62
Average yr of diagnosis of first cancer	1963	1966	1963
Person-yr of follow-up	4,853	2,118	6,971
Average follow-up, yr	3.0	4.4	3.3
Percent given radiotherapy for first cancer	66.5	52.6	63.3

[a] ICD-O code = 141.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the tongue in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	177	89.4
Only the first cancer	17	8.6
Only the second cancer	2	1.0
Neither first nor second cancer	2	1.0
Total second primary cancers	198	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

TONGUE
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the tongue among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	2,120			1,354			444			194			2,120		
Person-yr in interval	1,420			2,865			1,484			1,202			6,971		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**37**	**15.66**	**2.4**[b]	**82**	**33.04**	**2.5**[b]	**41**	**18.94**	**2.2**[b]	**38**	**18.24**	**2.1**[b]	**198**	**85.81**	**2.3**[b]
All excluding site of initial cancer	**36**	**15.50**	**2.3**[b]	**78**	**32.73**	**2.4**[b]	**39**	**18.78**	**2.1**[b]	**38**	**18.10**	**2.1**[b]	**191**	**85.03**	**2.2**[b]
Buccal cavity, pharynx	**8**	**0.78**	**10.2**[b]	**20**	**1.52**	**13.1**[b]	**8**	**0.82**	**9.8**[b]	**3**	**0.73**	**4.1**	**39**	**3.85**	**10.1**[b]
Lip	0	0.14	0.0	1	0.27	3.7	0	0.14	0.0	0	0.13	0.0	1	0.68	1.5
Tongue	1	0.16	6.1	4	0.31	13.0[b]	2	0.16	12.3[b]	0	0.14	0.0	7	0.78	9.0[b]
Salivary gland	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	1	0.05	22.1	1	0.22	4.6
Gum, other mouth	4	0.22	18.4[b]	10	0.43	23.2[b]	3	0.23	12.9[b]	1	0.21	4.8	18	1.09	16.6[b]
Pharynx	3	0.18	16.2[b]	3	0.37	8.1[b]	3	0.20	15.0[b]	1	0.18	5.6	10	0.93	10.7[b]
Digestive system	**17**	**5.14**	**3.3**[b]	**27**	**10.67**	**2.5**[b]	**13**	**6.15**	**2.1**[b]	**11**	**5.78**	**1.9**	**68**	**27.73**	**2.5**[b]
Esophagus	5	0.32	15.5[b]	13	0.63	20.5[b]	3	0.35	8.7[b]	4	0.31	13.0[b]	25	1.61	15.5[b]
Stomach	1	0.99	1.0	5	1.94	2.6	3	1.09	2.7	2	0.94	2.1	11	4.97	2.2[b]
Colon	5	1.89	2.6	5	4.07	1.2	4	2.40	1.7	4	2.37	1.7	18	10.73	1.7
Rectum	2	1.05	1.9	2	2.17	0.9	2	1.24	1.6	0	1.15	0.0	6	5.61	1.1
Liver, biliary	2	0.27	7.3	1	0.58	1.7	1	0.34	2.9	0	0.32	0.0	4	1.51	2.6
Pancreas	2	0.51	3.9	1	1.07	0.9	0	0.62	0.0	1	0.60	1.7	4	2.80	1.4
Respiratory system	**3**	**2.66**	**1.1**	**19**	**5.47**	**3.5**[b]	**7**	**3.02**	**2.3**	**13**	**2.98**	**4.4**[b]	**42**	**14.11**	**3.0**[b]
Nasal cavities, sinuses	0	0.03	0.0	1	0.07	14.1	0	0.04	0.0	0	0.04	0.0	1	0.18	5.5
Larynx	0	0.32	0.0	2	0.63	3.2	1	0.34	3.0	2	0.30	6.6	5	1.59	3.1[b]
Trachea, bronchus, lung	3	2.28	1.3	16	4.72	3.4[b]	6	2.61	2.3	11	2.61	4.2[b]	36	12.21	2.9[b]
Female breast	2	0.79	2.5	1	2.09	0.5	2	1.28	1.6	0	1.09	0.0	5	5.25	1.0
Female genital tract	**1**	**0.50**	**2.0**	**1**	**1.31**	**0.8**	**1**	**0.77**	**1.3**	**1**	**0.63**	**1.6**	**4**	**3.21**	**1.2**
Cervix uteri	0	0.10	0.0	0	0.24	0.0	0	0.13	0.0	1	0.10	10.5	1	0.57	1.8
Corpus uteri	1	0.20	4.9	0	0.54	0.0	0	0.32	0.0	0	0.29	0.0	1	1.35	0.7
Uterus, NOS	0	0.04	0.0	0	0.09	0.0	0	0.05	0.0	0	0.03	0.0	0	0.22	0.0
Ovary, fallopian tubes	0	0.14	0.0	0	0.36	0.0	1	0.21	4.8	0	0.18	0.0	1	0.88	1.1
Prostate gland	3	2.14	1.4	5	4.36	1.1	3	2.58	1.2	5	2.82	1.8	16	11.88	1.3
Testis	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Kidney, renal pelvis, ureter	0	0.36	0.0	3	0.75	4.0	0	0.42	0.0	0	0.40	0.0	3	1.93	1.6
Bladder, other urinary	0	0.96	0.0	1	1.98	0.5	4	1.14	3.5	1	1.17	0.9	6	5.24	1.1
Melanoma of the skin	0	0.17	0.0	1	0.36	2.7	0	0.20	0.0	0	0.18	0.0	1	0.92	1.1
Eye	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Brain, central nervous system	0	0.17	0.0	0	0.35	0.0	1	0.18	5.5	0	0.16	0.0	1	0.85	1.2
Thyroid gland	0	0.06	0.0	0	0.13	0.0	1	0.07	14.2	0	0.06	0.0	1	0.31	3.2
Bone	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.13	0.0
Connective tissue	0	0.08	0.0	0	0.16	0.0	0	0.09	0.0	1	0.09	11.7	1	0.40	2.5
Lymphatic, hematopoietic system	**1**	**0.99**	**1.0**	**3**	**2.11**	**1.4**	**1**	**1.22**	**0.8**	**2**	**1.21**	**1.7**	**7**	**5.53**	**1.3**
Non-Hodgkin's lymphoma	0	0.33	0.0	2	0.72	2.8	1	0.41	2.4	2	0.40	5.0	5	1.86	2.7
Hodgkin's disease	0	0.08	0.0	0	0.16	0.0	0	0.08	0.0	0	0.07	0.0	0	0.40	0.0
Multiple myeloma	0	0.15	0.0	1	0.32	3.1	0	0.19	0.0	0	0.20	0.0	1	0.85	1.2
Leukemias	1	0.44	2.3	0	0.91	0.0	0	0.53	0.0	0	0.54	0.0	1	2.42	0.4
Chronic lymphocytic	1	0.13	7.4	0	0.29	0.0	0	0.17	0.0	0	0.18	0.0	1	0.77	1.3
Acute nonlymphocytic	0	0.12	0.0	0	0.25	0.0	0	0.15	0.0	0	0.16	0.0	0	0.68	0.0

[a] ICD-O code = 141.

[b] $P < .05$

TONGUE
MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the tongue among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	1,643			999			296			126			1,643		
Person-yr in interval	1,075			1,992			979			806			4,853		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**31**	**12.64**	**2.5**[b]	**60**	**24.95**	**2.4**[b]	**27**	**13.91**	**1.9**[b]	**26**	**13.97**	**1.9**[b]	**144**	**65.42**	**2.2**[b]
All excluding site of initial cancer	**30**	**12.49**	**2.4**[b]	**57**	**24.67**	**2.3**[b]	**25**	**13.77**	**1.8**[b]	**26**	**13.84**	**1.9**[b]	**138**	**64.72**	**2.1**[b]
Buccal cavity, pharynx	**7**	**0.73**	**9.6**[b]	**15**	**1.38**	**10.9**[b]	**5**	**0.73**	**6.9**[b]	**2**	**0.65**	**3.1**	**29**	**3.48**	**8.3**[b]
Lip	0	0.14	0.0	1	0.26	3.9	0	0.14	0.0	0	0.12	0.0	1	0.66	1.5
Tongue	1	0.15	6.7	3	0.28	10.8[b]	2	0.14	13.9[b]	0	0.13	0.0	6	0.70	8.6[b]
Salivary gland	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.17	0.0
Gum, other mouth	3	0.20	15.1[b]	8	0.38	21.0[b]	0	0.20	0.0	1	0.18	5.6	12	0.96	12.5[b]
Pharynx	3	0.17	17.4[b]	2	0.34	5.9	3	0.18	16.7[b]	1	0.16	6.2	9	0.85	10.6[b]
Digestive system	**16**	**4.22**	**3.8**[b]	**17**	**8.17**	**2.1**[b]	**8**	**4.55**	**1.8**	**7**	**4.46**	**1.6**	**48**	**21.39**	**2.2**[b]
Esophagus	4	0.30	13.2[b]	10	0.58	17.3[b]	1	0.31	3.2	4	0.28	14.3[b]	19	1.47	12.9[b]
Stomach	1	0.87	1.2	2	1.60	1.2	3	0.88	3.4	1	0.79	1.3	7	4.13	1.7
Colon	5	1.47	3.4[b]	2	2.90	0.7	2	1.66	1.2	2	1.72	1.2	11	7.74	1.4
Rectum	2	0.88	2.3	2	1.70	1.2	1	0.94	1.1	0	0.90	0.0	5	4.42	1.1
Liver, biliary	2	0.21	9.5[b]	1	0.41	2.4	1	0.23	4.3	0	0.23	0.0	4	1.09	3.7
Pancreas	2	0.42	4.7	0	0.83	0.0	0	0.46	0.0	0	0.46	0.0	2	2.17	0.9
Respiratory system	**3**	**2.47**	**1.2**	**18**	**4.95**	**3.6**[b]	**6**	**2.70**	**2.2**	**7**	**2.67**	**2.6**[b]	**34**	**12.78**	**2.7**[b]
Nasal cavities, sinuses	0	0.03	0.0	1	0.06	17.6	0	0.03	0.0	0	0.03	0.0	1	0.15	6.9
Larynx	0	0.31	0.0	2	0.60	3.4	1	0.32	3.1	1	0.29	3.5	4	1.51	2.6
Trachea, bronchus, lung	3	2.11	1.4	15	4.26	3.5[b]	5	2.32	2.2	6	2.33	2.6	29	11.01	2.6[b]
Prostate gland	3	2.14	1.4	5	4.36	1.1	3	2.58	1.2	5	2.82	1.8	16	11.88	1.3
Testis	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Kidney, renal pelvis, ureter	0	0.32	0.0	2	0.62	3.2	0	0.34	0.0	0	0.33	0.0	2	1.61	1.2
Bladder, other urinary	0	0.88	0.0	1	1.76	0.6	3	0.99	3.0	1	1.03	1.0	5	4.65	1.1
Melanoma of the skin	0	0.14	0.0	1	0.27	3.7	0	0.14	0.0	0	0.14	0.0	1	0.69	1.5
Eye	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Brain, central nervous system	0	0.14	0.0	0	0.26	0.0	1	0.14	7.4	0	0.12	0.0	1	0.65	1.5
Thyroid gland	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.03	0.0	0	0.17	0.0
Bone	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Connective tissue	0	0.06	0.0	0	0.12	0.0	0	0.07	0.0	1	0.07	14.5	1	0.32	3.1
Lymphatic, hematopoietic system	**1**	**0.81**	**1.2**	**1**	**1.60**	**0.6**	**1**	**0.89**	**1.1**	**2**	**0.92**	**2.2**	**5**	**4.22**	**1.2**
Non-Hodgkin's lymphoma	0	0.26	0.0	1	0.52	1.9	1	0.29	3.5	2	0.29	7.0	4	1.35	3.0
Hodgkin's disease	0	0.07	0.0	0	0.13	0.0	0	0.06	0.0	0	0.06	0.0	0	0.31	0.0
Multiple myeloma	0	0.12	0.0	0	0.23	0.0	0	0.13	0.0	0	0.14	0.0	0	0.62	0.0
Leukemias	1	0.37	2.7	0	0.72	0.0	0	0.41	0.0	0	0.43	0.0	1	1.93	0.5
Chronic lymphocytic	1	0.12	8.6	0	0.24	0.0	0	0.14	0.0	0	0.14	0.0	1	0.63	1.6
Acute nonlymphocytic	0	0.10	0.0	0	0.19	0.0	0	0.11	0.0	0	0.12	0.0	0	0.52	0.0

[a] ICD-O code = 141.

[b] $P < .05$

TONGUE
FEMALES

TABLE 2E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the tongue among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	477			355			148			68			477		
Person-yr in interval	345			873			505			395			2,118		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**6**	**3.02**	**2.0**	**22**	**8.09**	**2.7^b**	**14**	**5.03**	**2.8^b**	**12**	**4.27**	**2.8^b**	**54**	**20.40**	**2.6^b**
All excluding site of initial cancer	**6**	**3.01**	**2.0**	**21**	**8.06**	**2.6^b**	**14**	**5.01**	**2.8^b**	**12**	**4.25**	**2.8^b**	**53**	**20.32**	**2.6^b**
Buccal cavity, pharynx	**1**	**0.06**	**17.9**	**5**	**0.14**	**34.6^b**	**3**	**0.09**	**33.1^b**	**1**	**0.08**	**13.0**	**10**	**0.37**	**27.2^b**
Lip	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.02	0.0
Tongue	0	0.01	0.0	1	0.03	33.0	0	0.02	0.0	0	0.02	0.0	1	0.08	13.1
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	1	0.01	106.5^b	1	0.05	22.0
Gum, other mouth	1	0.02	53.9	2	0.05	40.3^b	3	0.03	94.0^b	0	0.03	0.0	6	0.13	47.0^b
Pharynx	0	0.01	0.0	1	0.03	31.0	0	0.02	0.0	0	0.02	0.0	1	0.08	12.2
Digestive system	**1**	**0.92**	**1.1**	**10**	**2.50**	**4.0^b**	**5**	**1.60**	**3.1^b**	**4**	**1.33**	**3.0**	**20**	**6.34**	**3.2^b**
Esophagus	1	0.02	47.5	3	0.06	54.1^b	2	0.04	56.3^b	0	0.03	0.0	6	0.14	42.3^b
Stomach	0	0.13	0.0	3	0.34	8.8^b	0	0.22	0.0	1	0.15	6.6	4	0.84	4.8^b
Colon	0	0.43	0.0	3	1.17	2.6	2	0.75	2.7	2	0.64	3.1	7	2.98	2.3
Rectum	0	0.17	0.0	0	0.47	0.0	1	0.30	3.3	0	0.25	0.0	1	1.19	0.8
Liver, biliary	0	0.06	0.0	0	0.17	0.0	0	0.11	0.0	0	0.08	0.0	0	0.42	0.0
Pancreas	0	0.09	0.0	1	0.25	4.1	0	0.16	0.0	1	0.14	7.0	2	0.64	3.1
Respiratory system	**0**	**0.19**	**0.0**	**1**	**0.51**	**2.0**	**1**	**0.32**	**3.1**	**6**	**0.31**	**19.6^b**	**8**	**1.33**	**6.0^b**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	1	0.02	57.7	1	0.08	13.0
Trachea, bronchus, lung	0	0.17	0.0	1	0.46	2.2	1	0.29	3.5	5	0.28	18.0^b	7	1.20	5.8^b
Female breast	2	0.79	2.5	1	2.09	0.5	2	1.28	1.6	0	1.09	0.0	5	5.25	1.0
Female genital tract	**1**	**0.50**	**2.0**	**1**	**1.31**	**0.8**	**1**	**0.77**	**1.3**	**1**	**0.63**	**1.6**	**4**	**3.21**	**1.2**
Cervix uteri	0	0.10	0.0	0	0.24	0.0	0	0.13	0.0	1	0.10	10.5	1	0.57	1.8
Corpus uteri	1	0.20	4.9	0	0.54	0.0	0	0.32	0.0	0	0.29	0.0	1	1.35	0.7
Uterus, NOS	0	0.04	0.0	0	0.09	0.0	0	0.05	0.0	0	0.03	0.0	0	0.22	0.0
Ovary, fallopian tubes	0	0.14	0.0	0	0.36	0.0	1	0.21	4.8	0	0.18	0.0	1	0.88	1.1
Kidney, renal pelvis, ureter	0	0.05	0.0	1	0.13	7.8	0	0.08	0.0	0	0.07	0.0	1	0.33	3.1
Bladder, other urinary	0	0.08	0.0	0	0.23	0.0	1	0.15	6.7	0	0.13	0.0	1	0.59	1.7
Melanoma of the skin	0	0.03	0.0	0	0.09	0.0	0	0.06	0.0	0	0.05	0.0	0	0.23	0.0
Eye	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Brain, central nervous system	0	0.03	0.0	0	0.08	0.0	0	0.05	0.0	0	0.04	0.0	0	0.20	0.0
Thyroid gland	0	0.02	0.0	0	0.06	0.0	1	0.03	29.3	0	0.03	0.0	1	0.14	7.1
Bone	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Lymphatic, hematopoietic system	**0**	**0.19**	**0.0**	**2**	**0.51**	**3.9**	**0**	**0.32**	**0.0**	**0**	**0.29**	**0.0**	**2**	**1.31**	**1.5**
Non-Hodgkin's lymphoma	0	0.07	0.0	1	0.19	5.2	0	0.12	0.0	0	0.11	0.0	1	0.50	2.0
Hodgkin's disease	0	0.01	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Multiple myeloma	0	0.03	0.0	1	0.09	11.6	0	0.06	0.0	0	0.05	0.0	1	0.23	4.4
Leukemias	0	0.07	0.0	0	0.19	0.0	0	0.12	0.0	0	0.11	0.0	0	0.49	0.0
Chronic lymphocytic	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.03	0.0	0	0.14	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0

[a] ICD-O code = 141.

[b] $P < .05$

SALIVARY GLAND
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the salivary gland, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	444	411	855
No. who developed a second primary cancer	32	33	65
Average age at diagnosis of first cancer, yr	58	55	56
Average yr of diagnosis of first cancer	1964	1963	1964
Person-yr of follow-up	2,747	3,541	6,288
Average follow-up, yr	6.2	8.6	7.4
Percent given radiotherapy for first cancer	37.2	23.4	30.5

[a] ICD-O code = 142.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the salivary gland in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	53	81.5
Only the first cancer	8	12.3
Only the second cancer	3	4.6
Neither first nor second cancer	1	1.5
Total second primary cancers	65	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

SALIVARY GLAND
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the salivary gland among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	855			682			406			234			855		
Person-yr in interval	626			2,017			1,576			2,069			6,288		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8**	**5.47**	**1.5**	**20**	**16.28**	**1.2**	**17**	**13.34**	**1.3**	**20**	**19.89**	**1.0**	**65**	**54.94**	**1.2**
All excluding site of initial cancer	**8**	**5.45**	**1.5**	**20**	**16.24**	**1.2**	**17**	**13.31**	**1.3**	**20**	**19.84**	**1.0**	**65**	**54.80**	**1.2**
Buccal cavity, pharynx	**0**	**0.22**	**0.0**	**1**	**0.61**	**1.7**	**2**	**0.47**	**4.3**	**2**	**0.63**	**3.2**	**5**	**1.92**	**2.6**
Lip	0	0.04	0.0	0	0.10	0.0	1	0.07	14.3	2	0.08	24.2^{b}	3	0.28	10.5^{b}
Tongue	0	0.04	0.0	1	0.12	8.4	0	0.09	0.0	0	0.12	0.0	1	0.38	2.6
Salivary gland	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.14	0.0
Gum, other mouth	0	0.06	0.0	0	0.18	0.0	0	0.14	0.0	0	0.20	0.0	0	0.57	0.0
Pharynx	0	0.05	0.0	0	0.15	0.0	1	0.11	8.7	0	0.15	0.0	1	0.47	2.1
Digestive system	**2**	**1.74**	**1.1**	**5**	**5.05**	**1.0**	**5**	**4.10**	**1.2**	**7**	**6.08**	**1.2**	**19**	**16.97**	**1.1**
Esophagus	0	0.09	0.0	0	0.25	0.0	0	0.19	0.0	0	0.25	0.0	0	0.78	0.0
Stomach	0	0.31	0.0	1	0.85	1.2	1	0.64	1.6	1	0.84	1.2	3	2.63	1.1
Colon	2	0.69	2.9	2	2.05	1.0	1	1.72	0.6	3	2.70	1.1	8	7.16	1.1
Rectum	0	0.35	0.0	1	1.01	1.0	3	0.83	3.6	0	1.20	0.0	4	3.38	1.2
Liver, biliary	0	0.10	0.0	0	0.29	0.0	0	0.24	0.0	1	0.36	2.8	1	0.99	1.0
Pancreas	0	0.17	0.0	0	0.51	0.0	0	0.41	0.0	2	0.63	3.2	2	1.72	1.2
Respiratory system	**1**	**0.76**	**1.3**	**5**	**2.21**	**2.3**	**3**	**1.76**	**1.7**	**7**	**2.45**	**2.9**^{b}	**16**	**7.18**	**2.2**^{b}
Nasal cavities, sinuses	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.04	0.0	0	0.11	0.0
Larynx	0	0.08	0.0	1	0.24	4.2	0	0.19	0.0	1	0.23	4.3	2	0.74	2.7
Trachea, bronchus, lung	1	0.66	1.5	4	1.92	2.1	3	1.53	2.0	6	2.16	2.8^{b}	14	6.27	2.2^{b}
Female breast	2	0.55	3.7	3	1.89	1.6	1	1.67	0.6	2	3.00	0.7	8	7.10	1.1
Female genital tract	**1**	**0.36**	**2.8**	**2**	**1.23**	**1.6**	**1**	**1.04**	**1.0**	**1**	**1.71**	**0.6**	**5**	**4.34**	**1.2**
Cervix uteri	0	0.08	0.0	0	0.27	0.0	0	0.22	0.0	0	0.29	0.0	0	0.87	0.0
Corpus uteri	0	0.13	0.0	1	0.47	2.1	0	0.41	0.0	0	0.74	0.0	1	1.75	0.6
Uterus, NOS	0	0.03	0.0	0	0.09	0.0	0	0.07	0.0	0	0.08	0.0	0	0.27	0.0
Ovary, fallopian tubes	1	0.10	10.4	1	0.33	3.0	1	0.29	3.5	1	0.48	2.1	4	1.20	3.3
Prostate gland	1	0.61	1.6	1	1.65	0.6	3	1.30	2.3	0	1.55	0.0	5	5.11	1.0
Testis	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Kidney, renal pelvis, ureter	0	0.11	0.0	0	0.34	0.0	0	0.27	0.0	0	0.40	0.0	0	1.12	0.0
Bladder, other urinary	1	0.30	3.4	1	0.84	1.2	0	0.68	0.0	0	0.97	0.0	2	2.78	0.7
Melanoma of the skin	0	0.06	0.0	0	0.20	0.0	0	0.17	0.0	0	0.27	0.0	0	0.71	0.0
Eye	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Brain, central nervous system	0	0.06	0.0	0	0.18	0.0	0	0.15	0.0	0	0.21	0.0	0	0.59	0.0
Thyroid gland	0	0.03	0.0	0	0.09	0.0	0	0.08	0.0	0	0.11	0.0	0	0.30	0.0
Bone	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Connective tissue	0	0.03	0.0	0	0.08	0.0	0	0.07	0.0	0	0.09	0.0	0	0.26	0.0
Lymphatic, hematopoietic system	**0**	**0.35**	**0.0**	**0**	**1.06**	**0.0**	**2**	**0.89**	**2.3**	**0**	**1.38**	**0.0**	**2**	**3.68**	**0.5**
Non-Hodgkin's lymphoma	0	0.12	0.0	0	0.37	0.0	1	0.31	3.3	0	0.49	0.0	1	1.28	0.8
Hodgkin's disease	0	0.03	0.0	0	0.09	0.0	0	0.07	0.0	0	0.10	0.0	0	0.30	0.0
Multiple myeloma	0	0.05	0.0	0	0.16	0.0	0	0.14	0.0	0	0.23	0.0	0	0.59	0.0
Leukemias	0	0.15	0.0	0	0.44	0.0	1	0.37	2.7	0	0.56	0.0	1	1.52	0.7
Chronic lymphocytic	0	0.04	0.0	0	0.13	0.0	0	0.11	0.0	0	0.17	0.0	0	0.46	0.0
Acute nonlymphocytic	0	0.04	0.0	0	0.13	0.0	1	0.12	8.7	0	0.18	0.0	1	0.48	2.1

[a] ICD-O code = 142.

[b] $P < .05$

SALIVARY GLAND
MALES

TABLE 3D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the salivary gland among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	444			342			181			101			444		
Person-yr in interval	322			940			698			787			2,747		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**3.38**	**0.6**	**11**	**9.17**	**1.2**	**9**	**7.08**	**1.3**	**10**	**8.40**	**1.2**	**32**	**28.02**	**1.1**
All excluding site of initial cancer	**2**	**3.37**	**0.6**	**11**	**9.14**	**1.2**	**9**	**7.06**	**1.3**	**10**	**8.38**	**1.2**	**32**	**27.94**	**1.1**
Buccal cavity, pharynx	**0**	**0.18**	**0.0**	**1**	**0.48**	**2.1**	**1**	**0.36**	**2.8**	**2**	**0.43**	**4.7**	**4**	**1.45**	**2.8**
Lip	0	0.03	0.0	0	0.09	0.0	1	0.06	15.8	2	0.07	28.3[b]	3	0.26	11.7[b]
Tongue	0	0.04	0.0	1	0.10	10.5	0	0.07	0.0	0	0.08	0.0	1	0.28	3.5
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Gum, other mouth	0	0.05	0.0	0	0.13	0.0	0	0.10	0.0	0	0.13	0.0	0	0.41	0.0
Pharynx	0	0.04	0.0	0	0.12	0.0	0	0.09	0.0	0	0.11	0.0	0	0.36	0.0
Digestive system	**0**	**1.10**	**0.0**	**3**	**2.96**	**1.0**	**2**	**2.25**	**0.9**	**3**	**2.56**	**1.2**	**8**	**8.86**	**0.9**
Esophagus	0	0.08	0.0	0	0.20	0.0	0	0.15	0.0	0	0.17	0.0	0	0.59	0.0
Stomach	0	0.22	0.0	1	0.57	1.8	0	0.40	0.0	1	0.44	2.3	2	1.63	1.2
Colon	0	0.40	0.0	1	1.08	0.9	0	0.84	0.0	1	0.98	1.0	2	3.29	0.6
Rectum	0	0.23	0.0	0	0.61	0.0	2	0.47	4.3	0	0.53	0.0	2	1.84	1.1
Liver, biliary	0	0.06	0.0	0	0.15	0.0	0	0.12	0.0	0	0.13	0.0	0	0.45	0.0
Pancreas	0	0.11	0.0	0	0.30	0.0	0	0.23	0.0	1	0.26	3.8	1	0.90	1.1
Respiratory system	**1**	**0.65**	**1.5**	**5**	**1.79**	**2.8**	**3**	**1.39**	**2.2**	**5**	**1.70**	**2.9**	**14**	**5.53**	**2.5**[b]
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.06	0.0
Larynx	0	0.08	0.0	1	0.21	4.7	0	0.16	0.0	1	0.19	5.2	2	0.64	3.1
Trachea, bronchus, lung	1	0.56	1.8	4	1.54	2.6	3	1.20	2.5	4	1.48	2.7	12	4.78	2.5[b]
Prostate gland	1	0.61	1.6	1	1.65	0.6	3	1.30	2.3	0	1.55	0.0	5	5.11	1.0
Testis	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Kidney, renal pelvis, ureter	0	0.08	0.0	0	0.23	0.0	0	0.18	0.0	0	0.21	0.0	0	0.71	0.0
Bladder, other urinary	0	0.24	0.0	0	0.65	0.0	0	0.51	0.0	0	0.63	0.0	0	2.03	0.0
Melanoma of the skin	0	0.04	0.0	0	0.11	0.0	0	0.09	0.0	0	0.12	0.0	0	0.36	0.0
Eye	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Brain, central nervous system	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	0	0.10	0.0	0	0.32	0.0
Thyroid gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Connective tissue	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.04	0.0	0	0.15	0.0
Lymphatic, hematopoietic system	**0**	**0.22**	**0.0**	**0**	**0.61**	**0.0**	**0**	**0.48**	**0.0**	**0**	**0.58**	**0.0**	**0**	**1.89**	**0.0**
Non-Hodgkin's lymphoma	0	0.07	0.0	0	0.20	0.0	0	0.15	0.0	0	0.20	0.0	0	0.62	0.0
Hodgkin's disease	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Multiple myeloma	0	0.03	0.0	0	0.09	0.0	0	0.07	0.0	0	0.09	0.0	0	0.27	0.0
Leukemias	0	0.10	0.0	0	0.27	0.0	0	0.22	0.0	0	0.25	0.0	0	0.84	0.0
Chronic lymphocytic	0	0.03	0.0	0	0.08	0.0	0	0.07	0.0	0	0.08	0.0	0	0.27	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.07	0.0	0	0.24	0.0

[a] ICD-O code = 142.

[b] $P < .05$

SALIVARY GLAND FEMALES

TABLE 3E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the salivary gland among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	411			340			225			133			411		
Person-yr in interval	304			1,077			878			1,282			3,541		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**6**	**2.09**	**2.9**[b]	**9**	**7.10**	**1.3**	**8**	**6.25**	**1.3**	**10**	**11.49**	**0.9**	**33**	**26.92**	**1.2**
All excluding site of initial cancer	**6**	**2.08**	**2.9**[b]	**9**	**7.08**	**1.3**	**8**	**6.24**	**1.3**	**10**	**11.47**	**0.9**	**33**	**26.86**	**1.2**
Buccal cavity, pharynx	**0**	**0.04**	**0.0**	**0**	**0.12**	**0.0**	**1**	**0.11**	**9.1**	**0**	**0.20**	**0.0**	**1**	**0.47**	**2.1**
Lip	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Tongue	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.10	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Gum, other mouth	0	0.01	0.0	0	0.04	0.0	0	0.04	0.0	0	0.07	0.0	0	0.16	0.0
Pharynx	0	0.01	0.0	0	0.03	0.0	1	0.02	40.3	0	0.04	0.0	1	0.10	9.7
Digestive system	**2**	**0.64**	**3.1**	**2**	**2.10**	**1.0**	**3**	**1.85**	**1.6**	**4**	**3.52**	**1.1**	**11**	**8.10**	**1.4**
Esophagus	0	0.01	0.0	0	0.05	0.0	0	0.04	0.0	0	0.08	0.0	0	0.18	0.0
Stomach	0	0.09	0.0	0	0.28	0.0	1	0.23	4.3	0	0.39	0.0	1	1.00	1.0
Colon	2	0.29	6.8	1	0.97	1.0	1	0.87	1.1	2	1.73	1.2	6	3.86	1.6
Rectum	0	0.12	0.0	1	0.40	2.5	1	0.36	2.8	0	0.67	0.0	2	1.54	1.3
Liver, biliary	0	0.04	0.0	0	0.14	0.0	0	0.12	0.0	1	0.23	4.4	1	0.54	1.9
Pancreas	0	0.06	0.0	0	0.21	0.0	0	0.18	0.0	1	0.37	2.7	1	0.82	1.2
Respiratory system	**0**	**0.12**	**0.0**	**0**	**0.42**	**0.0**	**0**	**0.37**	**0.0**	**2**	**0.75**	**2.7**	**2**	**1.65**	**1.2**
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Larynx	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.10	0.0
Trachea, bronchus, lung	0	0.10	0.0	0	0.37	0.0	0	0.33	0.0	2	0.68	2.9	2	1.50	1.3
Female breast	2	0.55	3.7	3	1.89	1.6	1	1.67	0.6	2	3.00	0.7	8	7.10	1.1
Female genital tract	**1**	**0.36**	**2.8**	**2**	**1.23**	**1.6**	**1**	**1.04**	**1.0**	**1**	**1.71**	**0.6**	**5**	**4.34**	**1.2**
Cervix uteri	0	0.08	0.0	0	0.27	0.0	0	0.22	0.0	0	0.29	0.0	0	0.87	0.0
Corpus uteri	0	0.13	0.0	1	0.47	2.1	0	0.41	0.0	0	0.74	0.0	1	1.75	0.6
Uterus, NOS	0	0.03	0.0	0	0.09	0.0	0	0.07	0.0	0	0.08	0.0	0	0.27	0.0
Ovary, fallopian tubes	1	0.10	10.4	1	0.33	3.0	1	0.29	3.5	1	0.48	2.1	4	1.20	3.3
Kidney, renal pelvis, ureter	0	0.03	0.0	0	0.11	0.0	0	0.10	0.0	0	0.18	0.0	0	0.42	0.0
Bladder, other urinary	1	0.06	18.2	1	0.19	5.4	0	0.17	0.0	0	0.34	0.0	2	0.75	2.7
Melanoma of the skin	0	0.03	0.0	0	0.09	0.0	0	0.08	0.0	0	0.15	0.0	0	0.35	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Brain, central nervous system	0	0.02	0.0	0	0.07	0.0	0	0.07	0.0	0	0.11	0.0	0	0.27	0.0
Thyroid gland	0	0.02	0.0	0	0.06	0.0	0	0.05	0.0	0	0.09	0.0	0	0.22	0.0
Bone	0	0.0	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.05	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**0**	**0.13**	**0.0**	**0**	**0.45**	**0.0**	**2**	**0.41**	**4.9**	**0**	**0.80**	**0.0**	**2**	**1.79**	**1.1**
Non-Hodgkin's lymphoma	0	0.05	0.0	0	0.17	0.0	1	0.15	6.6	0	0.30	0.0	1	0.66	1.5
Hodgkin's disease	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.14	0.0
Multiple myeloma	0	0.02	0.0	0	0.07	0.0	0	0.07	0.0	0	0.15	0.0	0	0.31	0.0
Leukemias	0	0.05	0.0	0	0.17	0.0	1	0.15	6.5	0	0.30	0.0	1	0.68	1.5
Chronic lymphocytic	0	0.01	0.0	0	0.05	0.0	0	0.04	0.0	0	0.09	0.0	0	0.19	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.06	0.0	1	0.05	19.1	0	0.11	0.0	1	0.23	4.3

[a] ICD-O code = 142.

[b] $P < .05$.

MOUTH
BOTH SEXES

TABLE 4A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the gum or other mouth, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,279	784	3,063
No. who developed a second primary cancer	328	96	424
Average age at diagnosis of first cancer, yr	63	62	63
Average yr of diagnosis of first cancer	1963	1967	1964
Person-yr of follow-up	8,478	4,000	12,478
Average follow-up, yr	3.7	5.1	4.1
Percent given radiotherapy for first cancer	58.6	49.0	56.2

[a] ICD-O codes = 143–145.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the gum or other mouth in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	369	87.0
Only the first cancer	42	9.9
Only the second cancer	9	2.1
Neither first nor second cancer	4	0.9
Total second primary cancers	424	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

MOUTH
BOTH SEXES

TABLE 4C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the gum or other mouth among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,063			2,179			831			375			3,063		
Person-yr in interval	2,158			5,134			2,837			2,349			12,478		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**65**	**24.48**	**2.7[b]**	**175**	**59.59**	**2.9[b]**	**93**	**36.66**	**2.5[b]**	**91**	**35.81**	**2.5[b]**	**424**	**156.44**	**2.7[b]**
All excluding site of initial cancer	**60**	**24.14**	**2.5[b]**	**155**	**58.80**	**2.6[b]**	**81**	**36.20**	**2.2[b]**	**78**	**35.42**	**2.2[b]**	**374**	**154.45**	**2.4[b]**
Buccal cavity, pharynx	**18**	**1.20**	**15.0[b]**	**50**	**2.77**	**18.1[b]**	**30**	**1.63**	**18.4[b]**	**30**	**1.37**	**21.9[b]**	**128**	**6.96**	**18.4[b]**
Lip	1	0.22	4.5	2	0.49	4.1	1	0.30	3.4	2	0.24	8.4	6	1.24	4.8[b]
Tongue	8	0.24	33.4[b]	12	0.56	21.5[b]	7	0.32	21.8[b]	6	0.26	23.0[b]	33	1.38	24.0[b]
Salivary gland	2	0.06	32.2[b]	2	0.15	13.6[b]	1	0.09	10.9	0	0.09	0.0	5	0.39	12.7[b]
Gum, other mouth	5	0.34	14.6[b]	20	0.79	25.2[b]	12	0.46	26.0[b]	13	0.39	32.9[b]	50	1.99	25.1[b]
Pharynx	0	0.28	0.0	10	0.67	15.0[b]	7	0.39	17.7[b]	9	0.33	27.3[b]	26	1.67	15.6[b]
Digestive system	**19**	**8.03**	**2.4[b]**	**42**	**19.19**	**2.2[b]**	**23**	**11.84**	**1.9[b]**	**19**	**11.31**	**1.7[b]**	**103**	**50.33**	**2.0[b]**
Esophagus	7	0.49	14.2[b]	12	1.15	10.4[b]	11	0.69	15.9[b]	5	0.57	8.8[b]	35	2.90	12.1[b]
Stomach	1	1.55	0.6	8	3.50	2.3	4	2.11	1.9	2	1.82	1.1	15	8.98	1.7
Colon	6	2.97	2.0	12	7.30	1.6	4	4.57	0.9	8	4.69	1.7	30	19.52	1.5[b]
Rectum	2	1.63	1.2	4	3.92	1.0	2	2.41	0.8	0	2.25	0.0	8	10.20	0.8
Liver, biliary	1	0.43	2.3	2	1.04	1.9	0	0.64	0.0	1	0.63	1.6	4	2.72	1.5
Pancreas	1	0.80	1.2	3	1.94	1.5	2	1.20	1.7	3	1.17	2.6	9	5.11	1.8
Respiratory system	**14**	**4.03**	**3.5[b]**	**38**	**9.94**	**3.8[b]**	**19**	**5.99**	**3.2[b]**	**17**	**5.52**	**3.1[b]**	**88**	**25.47**	**3.5[b]**
Nasal cavities, sinuses	1	0.05	19.0	1	0.12	8.1	0	0.08	0.0	1	0.07	14.2	3	0.32	9.3[b]
Larynx	3	0.48	6.2[b]	5	1.15	4.3[b]	3	0.68	4.4	2	0.54	3.7	13	2.85	4.6[b]
Trachea, bronchus, lung	10	3.46	2.9[b]	31	8.58	3.6[b]	16	5.19	3.1[b]	14	4.86	2.9[b]	71	22.07	3.2[b]
Female breast	0	1.36	0.0	7	3.67	1.9	2	2.26	0.9	4	2.53	1.6	13	9.81	1.3
Female genital tract	**1**	**0.84**	**1.2**	**5**	**2.28**	**2.2**	**1**	**1.38**	**0.7**	**2**	**1.49**	**1.3**	**9**	**5.99**	**1.5**
Cervix uteri	1	0.16	6.4	1	0.42	2.4	0	0.25	0.0	0	0.24	0.0	2	1.07	1.9
Corpus uteri	0	0.35	0.0	2	0.97	2.1	0	0.59	0.0	2	0.66	3.0	4	2.57	1.6
Uterus, NOS	0	0.06	0.0	0	0.15	0.0	0	0.09	0.0	0	0.08	0.0	0	0.38	0.0
Ovary, fallopian tubes	0	0.22	0.0	1	0.61	1.6	0	0.38	0.0	0	0.41	0.0	1	1.63	0.6
Prostate gland	6	3.38	1.8	16	7.99	2.0[b]	10	5.18	1.9	11	5.42	2.0[b]	43	21.96	2.0[b]
Testis	0	0.04	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.18	0.0
Kidney, renal pelvis, ureter	2	0.55	3.6	0	1.35	0.0	0	0.82	0.0	2	0.76	2.6	4	3.49	1.1
Bladder, other urinary	0	1.49	0.0	6	3.60	1.7	2	2.23	0.9	1	2.24	0.4	9	9.56	0.9
Melanoma of the skin	2	0.27	7.5	0	0.66	0.0	0	0.37	0.0	0	0.36	0.0	2	1.65	1.2
Eye	0	0.04	0.0	0	0.09	0.0	0	0.05	0.0	0	0.05	0.0	0	0.23	0.0
Brain, central nervous system	0	0.25	0.0	0	0.62	0.0	1	0.35	2.8	0	0.31	0.0	1	1.53	0.7
Thyroid gland	1	0.09	11.1	0	0.22	0.0	1	0.13	7.8	0	0.12	0.0	2	0.56	3.6
Bone	0	0.04	0.0	0	0.09	0.0	0	0.05	0.0	0	0.04	0.0	0	0.23	0.0
Connective tissue	0	0.12	0.0	1	0.29	3.5	0	0.17	0.0	0	0.16	0.0	1	0.74	1.4
Lymphatic, hematopoietic system	**0**	**1.55**	**0.0**	**3**	**3.81**	**0.8**	**3**	**2.35**	**1.3**	**3**	**2.38**	**1.3**	**9**	**10.07**	**0.9**
Non-Hodgkin's lymphoma	0	0.52	0.0	1	1.30	0.8	0	0.79	0.0	1	0.79	1.3	2	3.39	0.6
Hodgkin's disease	0	0.12	0.0	0	0.28	0.0	0	0.16	0.0	1	0.14	7.0	1	0.70	1.4
Multiple myeloma	0	0.23	0.0	0	0.58	0.0	0	0.37	0.0	1	0.39	2.5	1	1.57	0.6
Leukemias	0	0.68	0.0	2	1.65	1.2	3	1.03	2.9	0	1.06	0.0	5	4.41	1.1
Chronic lymphocytic	0	0.21	0.0	0	0.51	0.0	0	0.32	0.0	0	0.34	0.0	0	1.39	0.0
Acute nonlymphocytic	0	0.19	0.0	2	0.47	4.2	1	0.29	3.4	0	0.32	0.0	3	1.27	2.4

[a] ICD-O codes = 143–145.

[b] $P < .05$.

MOUTH
MALES

TABLE 4D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the gum or other mouth among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,279			1,566			567			252			2,279		
Person-yr in interval	1,582			3,583			1,915			1,398			8,478		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**58**	**19.32**	**3.0**[b]	**132**	**45.54**	**2.9**[b]	**67**	**27.96**	**2.4**[b]	**71**	**25.72**	**2.8**[b]	**328**	**118.46**	**2.8**[b]
All excluding site of initial cancer	**53**	**19.01**	**2.8**[b]	**121**	**44.84**	**2.7**[b]	**61**	**27.55**	**2.2**[b]	**61**	**25.39**	**2.4**[b]	**296**	**116.71**	**2.5**[b]
Buccal cavity, pharynx	**17**	**1.10**	**15.4**[b]	**34**	**2.51**	**13.6**[b]	**17**	**1.47**	**11.6**[b]	**24**	**1.19**	**20.2**[b]	**92**	**6.26**	**14.7**[b]
Lip	1	0.22	4.6	2	0.48	4.2	1	0.29	3.5	2	0.23	8.8	6	1.21	5.0[b]
Tongue	8	0.22	36.2[b]	9	0.50	17.8[b]	2	0.29	6.9	5	0.22	22.3[b]	24	1.24	19.4[b]
Salivary gland	1	0.05	19.6	2	0.12	17.1[b]	0	0.07	0.0	0	0.07	0.0	3	0.31	9.6[b]
Gum, other mouth	5	0.31	16.3[b]	11	0.70	15.6[b]	6	0.41	14.8[b]	10	0.33	30.3[b]	32	1.75	18.3[b]
Pharynx	0	0.26	0.0	7	0.61	11.5[b]	6	0.36	16.8[b]	7	0.29	24.1[b]	20	1.51	13.2[b]
Digestive system	**16**	**6.46**	**2.5**[b]	**35**	**14.96**	**2.3**[b]	**16**	**9.18**	**1.7**	**16**	**8.10**	**2.0**[b]	**83**	**38.67**	**2.1**[b]
Esophagus	6	0.46	13.1[b]	12	1.05	11.4[b]	10	0.63	15.9[b]	3	0.49	6.1[b]	31	2.63	11.8[b]
Stomach	1	1.34	0.7	8	2.95	2.7[b]	3	1.77	1.7	2	1.44	1.4	14	7.50	1.9[b]
Colon	4	2.24	1.8	6	5.31	1.1	1	3.32	0.3	7	3.15	2.2	18	14.01	1.3
Rectum	2	1.34	1.5	4	3.11	1.3	1	1.91	0.5	0	1.64	0.0	7	7.99	0.9
Liver, biliary	1	0.32	3.1	2	0.75	2.7	0	0.47	0.0	1	0.42	2.4	4	1.96	2.0
Pancreas	1	0.64	1.6	2	1.51	1.3	1	0.93	1.1	3	0.83	3.6	7	3.92	1.8
Respiratory system	**13**	**3.70**	**3.5**[b]	**33**	**8.99**	**3.7**[b]	**19**	**5.39**	**3.5**[b]	**13**	**4.82**	**2.7**[b]	**78**	**22.89**	**3.4**[b]
Nasal cavities, sinuses	1	0.04	22.9	0	0.10	0.0	0	0.06	0.0	1	0.05	18.6	2	0.26	7.7
Larynx	3	0.46	6.5[b]	4	1.10	3.6	3	0.64	4.7	1	0.51	2.0	11	2.70	4.1[b]
Trachea, bronchus, lung	9	3.16	2.8[b]	28	7.72	3.6[b]	16	4.65	3.4[b]	11	4.22	2.6[b]	64	19.73	3.2[b]
Prostate gland	6	3.38	1.8	16	7.99	2.0[b]	10	5.18	1.9	11	5.42	2.0[b]	43	21.96	2.0[b]
Testis	0	0.04	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.18	0.0
Kidney, renal pelvis, ureter	2	0.47	4.2	0	1.13	0.0	0	0.68	0.0	2	0.60	3.3	4	2.89	1.4
Bladder, other urinary	0	1.35	0.0	5	3.21	1.6	2	1.99	1.0	0	1.93	0.0	7	8.47	0.8
Melanoma of the skin	2	0.21	9.7[b]	0	0.49	0.0	0	0.28	0.0	0	0.25	0.0	2	1.22	1.6
Eye	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.03	0.0	0	0.17	0.0
Brain, central nervous system	0	0.20	0.0	0	0.48	0.0	0	0.26	0.0	0	0.21	0.0	0	1.15	0.0
Thyroid gland	1	0.05	18.5	0	0.13	0.0	0	0.07	0.0	0	0.06	0.0	1	0.31	3.2
Bone	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.03	0.0	0	0.18	0.0
Connective tissue	0	0.10	0.0	1	0.23	4.4	0	0.14	0.0	0	0.12	0.0	1	0.58	1.7
Lymphatic, hematopoietic system	**0**	**1.23**	**0.0**	**2**	**2.93**	**0.7**	**2**	**1.79**	**1.1**	**3**	**1.69**	**1.8**	**7**	**7.63**	**0.9**
Non-Hodgkin's lymphoma	0	0.40	0.0	1	0.95	1.0	0	0.57	0.0	1	0.52	1.9	2	2.45	0.8
Hodgkin's disease	0	0.10	0.0	0	0.22	0.0	0	0.13	0.0	1	0.10	10.0	1	0.54	1.8
Multiple myeloma	0	0.17	0.0	0	0.42	0.0	0	0.27	0.0	1	0.27	3.8	1	1.13	0.9
Leukemias	0	0.56	0.0	1	1.33	0.8	2	0.82	2.4	0	0.80	0.0	3	3.51	0.9
Chronic lymphocytic	0	0.18	0.0	0	0.42	0.0	0	0.27	0.0	0	0.26	0.0	0	1.13	0.0
Acute nonlymphocytic	0	0.15	0.0	1	0.36	2.8	1	0.22	4.5	0	0.24	0.0	2	0.97	2.1

[a] ICD-O codes =143–145.
[b] $P < .05$.

MOUTH
FEMALES

TABLE 4E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the gum or other mouth among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	784			613			264			123			784		
Person-yr in interval	576			1,551			922			951			4,000		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**7**	**5.16**	**1.4**	**43**	**14.04**	**3.1**[b]	**26**	**8.70**	**3.0**[b]	**20**	**10.09**	**2.0**[b]	**96**	**37.97**	**2.5**[b]
All excluding site of initial cancer	**7**	**5.13**	**1.4**	**34**	**13.95**	**2.4**[b]	**20**	**8.64**	**2.3**[b]	**17**	**10.03**	**1.7**	**78**	**37.72**	**2.1**[b]
Buccal cavity, pharynx	**1**	**0.10**	**10.5**	**16**	**0.26**	**61.5**[b]	**13**	**0.16**	**81.5**[b]	**6**	**0.18**	**33.3**[b]	**36**	**0.69**	**51.8**[b]
Lip	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Tongue	0	0.02	0.0	3	0.05	57.4[b]	5	0.03	151.2[b]	1	0.04	27.2	9	0.14	63.8[b]
Salivary gland	1	0.01	90.5[b]	0	0.03	0.0	1	0.02	54.6	0	0.02	0.0	2	0.08	24.6[b]
Gum, other mouth	0	0.03	0.0	9	0.09	98.9[b]	6	0.06	107.8[b]	3	0.06	46.2[b]	18	0.25	73.3[b]
Pharynx	0	0.02	0.0	3	0.06	49.7[b]	1	0.04	27.3	2	0.04	50.2[b]	6	0.16	38.0[b]
Digestive system	**3**	**1.57**	**1.9**	**7**	**4.24**	**1.7**	**7**	**2.65**	**2.6**[b]	**3**	**3.20**	**0.9**	**20**	**11.66**	**1.7**[b]
Esophagus	1	0.04	26.7	0	0.10	0.0	1	0.06	15.9	2	0.07	27.2[b]	4	0.27	14.6[b]
Stomach	0	0.21	0.0	0	0.55	0.0	1	0.34	3.0	0	0.38	0.0	1	1.48	0.7
Colon	2	0.73	2.8	6	1.99	3.0[b]	3	1.25	2.4	1	1.55	0.6	12	5.51	2.2[b]
Rectum	0	0.30	0.0	0	0.81	0.0	1	0.51	2.0	0	0.61	0.0	1	2.22	0.5
Liver, biliary	0	0.10	0.0	0	0.28	0.0	0	0.17	0.0	0	0.21	0.0	0	0.77	0.0
Pancreas	0	0.16	0.0	1	0.43	2.3	1	0.27	3.7	0	0.33	0.0	2	1.19	1.7
Respiratory system	**1**	**0.34**	**3.0**	**5**	**0.95**	**5.3**[b]	**0**	**0.59**	**0.0**	**4**	**0.70**	**5.7**[b]	**10**	**2.58**	**3.9**[b]
Nasal cavities, sinuses	0	0.01	0.0	1	0.02	41.7	0	0.01	0.0	0	0.02	0.0	1	0.06	15.6
Larynx	0	0.02	0.0	1	0.06	17.6	0	0.03	0.0	1	0.04	27.0	2	0.15	13.5[b]
Trachea, bronchus, lung	1	0.30	3.3	3	0.86	3.5	0	0.54	0.0	3	0.63	4.7	7	2.33	3.0[b]
Female breast	0	1.36	0.0	7	3.67	1.9	2	2.26	0.9	4	2.53	1.6	13	9.81	1.3
Female genital tract	**1**	**0.84**	**1.2**	**5**	**2.28**	**2.2**	**1**	**1.38**	**0.7**	**2**	**1.49**	**1.3**	**9**	**5.99**	**1.5**
Cervix uteri	1	0.16	6.4	1	0.42	2.4	0	0.25	0.0	0	0.24	0.0	2	1.07	1.9
Corpus uteri	0	0.35	0.0	2	0.97	2.1	0	0.59	0.0	2	0.66	3.0	4	2.57	1.6
Uterus, NOS	0	0.06	0.0	0	0.15	0.0	0	0.09	0.0	0	0.08	0.0	0	0.38	0.0
Ovary, fallopian tubes	0	0.22	0.0	1	0.61	1.6	0	0.38	0.0	0	0.41	0.0	1	1.63	0.6
Kidney, renal pelvis, ureter	0	0.08	0.0	0	0.22	0.0	0	0.14	0.0	0	0.17	0.0	0	0.60	0.0
Bladder, other urinary	0	0.15	0.0	1	0.40	2.5	0	0.25	0.0	1	0.31	3.3	2	1.10	1.8
Melanoma of the skin	0	0.06	0.0	0	0.17	0.0	0	0.10	0.0	0	0.11	0.0	0	0.44	0.0
Eye	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Brain, central nervous system	0	0.05	0.0	0	0.14	0.0	1	0.09	11.3	0	0.10	0.0	1	0.38	2.6
Thyroid gland	0	0.04	0.0	0	0.10	0.0	1	0.06	17.6	0	0.06	0.0	1	0.25	4.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.02	0.0	0	0.06	0.0	0	0.03	0.0	0	0.04	0.0	0	0.15	0.0
Lymphatic, hematopoietic system	**0**	**0.32**	**0.0**	**1**	**0.88**	**1.1**	**1**	**0.56**	**1.8**	**0**	**0.69**	**0.0**	**2**	**2.44**	**0.8**
Non-Hodgkin's lymphoma	0	0.12	0.0	0	0.34	0.0	0	0.22	0.0	0	0.26	0.0	0	0.95	0.0
Hodgkin's disease	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Multiple myeloma	0	0.05	0.0	0	0.15	0.0	0	0.10	0.0	0	0.13	0.0	0	0.43	0.0
Leukemias	0	0.12	0.0	1	0.32	3.1	1	0.21	4.9	0	0.25	0.0	2	0.90	2.2
Chronic lymphocytic	0	0.03	0.0	0	0.09	0.0	0	0.06	0.0	0	0.08	0.0	0	0.26	0.0
Acute nonlymphocytic	0	0.04	0.0	1	0.11	9.1	0	0.07	0.0	0	0.09	0.0	1	0.31	3.2

[a] ICD-O codes = 143–145.

[b] $P < .05$.

PHARYNX
BOTH SEXES

TABLE 5A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the pharynx, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,098	539	2,637
No. who developed a second primary cancer	178	30	208
Average age at diagnosis of first cancer, yr	61	59	60
Average yr of diagnosis of first cancer	1964	1967	1965
Person-yr of follow-up	5,267	1,757	7,024
Average follow-up, yr	2.5	3.3	2.7
Percent given radiotherapy for first cancer	85.6	84.8	85.4

[a] ICD-O codes = 146–148.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 5B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the pharynx in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	178	85.6
Only the first cancer	22	10.6
Only the second cancer	5	2.4
Neither first nor second cancer	3	1.4
Total second primary cancers	208	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

PHARYNX
BOTH SEXES

TABLE 5C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pharynx among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,637			1,549			417			165			2,637		
Person-yr in interval	1,686			3,025			1,331			983			7,024		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**43**	**17.79**	**2.4**[b]	**97**	**33.97**	**2.9**[b]	**50**	**17.07**	**2.9**[b]	**18**	**13.63**	**1.3**	**208**	**82.40**	**2.5**[b]
All excluding site of initial cancer	**43**	**17.56**	**2.4**[b]	**90**	**33.56**	**2.7**[b]	**47**	**16.89**	**2.8**[b]	**17**	**13.49**	**1.3**	**197**	**81.43**	**2.4**[b]
Buccal cavity, pharynx	**8**	**0.90**	**8.9**[b]	**19**	**1.61**	**11.8**[b]	**10**	**0.73**	**13.6**[b]	**4**	**0.55**	**7.3**[b]	**41**	**3.79**	**10.8**[b]
Lip	0	0.15	0.0	1	0.26	3.8	0	0.12	0.0	0	0.08	0.0	1	0.62	1.6
Tongue	4	0.18	22.1[b]	4	0.33	12.2[b]	4	0.15	27.4[b]	1	0.11	9.4	13	0.76	17.1[b]
Salivary gland	0	0.05	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.20	0.0
Gum, other mouth	3	0.25	11.8[b]	7	0.46	15.2[b]	2	0.21	9.4[b]	2	0.16	12.2[b]	14	1.09	12.8[b]
Pharynx	0	0.23	0.0	7	0.41	16.9[b]	3	0.18	16.3[b]	1	0.14	7.3	11	0.97	11.4[b]
Digestive system	**16**	**5.62**	**2.8**[b]	**31**	**10.55**	**2.9**[b]	**15**	**5.36**	**2.8**[b]	**3**	**4.20**	**0.7**	**65**	**25.72**	**2.5**[b]
Esophagus	8	0.37	21.7[b]	12	0.67	18.0[b]	4	0.31	12.9[b]	1	0.23	4.4	25	1.57	15.9[b]
Stomach	0	1.04	0.0	5	1.82	2.7	2	0.89	2.3	0	0.64	0.0	7	4.38	1.6
Colon	4	2.07	1.9	6	4.02	1.5	4	2.13	1.9	2	1.74	1.2	16	9.95	1.6
Rectum	1	1.18	0.8	5	2.21	2.3	1	1.10	0.9	0	0.86	0.0	7	5.34	1.3
Liver, biliary	1	0.29	3.4	2	0.57	3.5	2	0.29	6.9	0	0.22	0.0	5	1.37	3.6[b]
Pancreas	2	0.57	3.5	1	1.09	0.9	2	0.55	3.6	0	0.44	0.0	5	2.65	1.9
Respiratory system	**5**	**3.33**	**1.5**	**29**	**6.36**	**4.6**[b]	**14**	**3.04**	**4.6**[b]	**4**	**2.45**	**1.6**	**52**	**15.17**	**3.4**[b]
Nasal cavities, sinuses	0	0.04	0.0	1	0.07	14.1	0	0.03	0.0	0	0.03	0.0	1	0.17	5.9
Larynx	0	0.39	0.0	8	0.72	11.1[b]	3	0.33	9.2[b]	2	0.25	8.0	13	1.69	7.7[b]
Trachea, bronchus, lung	5	2.87	1.7	20	5.51	3.6[b]	11	2.65	4.1[b]	2	2.15	0.9	38	13.17	2.9[b]
Female breast	3	0.77	3.9	2	1.69	1.2	2	0.91	2.2	0	0.71	0.0	7	4.08	1.7
Female genital tract	**0**	**0.50**	**0.0**	**1**	**1.09**	**0.9**	**0**	**0.57**	**0.0**	**0**	**0.41**	**0.0**	**1**	**2.56**	**0.4**
Cervix uteri	0	0.10	0.0	0	0.20	0.0	0	0.10	0.0	0	0.07	0.0	0	0.46	0.0
Corpus uteri	0	0.21	0.0	1	0.48	2.1	0	0.25	0.0	0	0.18	0.0	1	1.13	0.9
Uterus, NOS	0	0.03	0.0	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.15	0.0
Ovary, fallopian tubes	0	0.13	0.0	0	0.29	0.0	0	0.15	0.0	0	0.11	0.0	0	0.69	0.0
Prostate gland	4	2.45	1.6	6	4.65	1.3	5	2.46	2.0	2	2.10	1.0	17	11.66	1.5
Testis	0	0.03	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.12	0.0
Kidney, renal pelvis, ureter	1	0.43	2.3	2	0.82	2.4	0	0.40	0.0	1	0.31	3.2	4	1.96	2.0
Bladder, other urinary	2	1.12	1.8	1	2.12	0.5	1	1.08	0.9	0	0.89	0.0	4	5.21	0.8
Melanoma of the skin	0	0.21	0.0	0	0.40	0.0	0	0.19	0.0	0	0.16	0.0	0	0.96	0.0
Eye	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.13	0.0
Brain, central nervous system	0	0.21	0.0	0	0.39	0.0	0	0.18	0.0	0	0.14	0.0	0	0.91	0.0
Thyroid gland	0	0.07	0.0	0	0.13	0.0	0	0.06	0.0	0	0.05	0.0	0	0.30	0.0
Bone	0	0.03	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.12	0.0
Connective tissue	0	0.09	0.0	1	0.16	6.2	0	0.08	0.0	1	0.06	15.9	2	0.39	5.1
Lymphatic, hematopoietic system	**2**	**1.15**	**1.7**	**4**	**2.21**	**1.8**	**2**	**1.12**	**1.8**	**1**	**0.91**	**1.1**	**9**	**5.38**	**1.7**
Non-Hodgkin's lymphoma	1	0.40	2.5	1	0.76	1.3	1	0.38	2.6	1	0.31	3.3	4	1.84	2.2
Hodgkin's disease	0	0.09	0.0	0	0.17	0.0	0	0.08	0.0	0	0.06	0.0	0	0.40	0.0
Multiple myeloma	0	0.17	0.0	0	0.34	0.0	0	0.18	0.0	0	0.15	0.0	0	0.84	0.0
Leukemias	1	0.49	2.0	3	0.94	3.2	1	0.48	2.1	0	0.40	0.0	5	2.30	2.2
Chronic lymphocytic	1	0.15	6.5	1	0.29	3.4	0	0.16	0.0	0	0.13	0.0	2	0.73	2.7
Acute nonlymphocytic	0	0.14	0.0	1	0.28	3.6	0	0.15	0.0	0	0.13	0.0	1	0.69	1.4

[a] ICD-O codes = 146–148.
[b] $P < .05$.

PHARYNX
MALES

TABLE 5D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pharynx among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,098			1,212			301			116			2,098		
Person-yr in interval	1,332			2,278			958			700			5,267		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**38**	**15.02**	**2.5**[b]	**83**	**27.71**	**3.0**[b]	**45**	**13.46**	**3.3**[b]	**12**	**10.83**	**1.1**	**178**	**66.96**	**2.7**[b]
All excluding site of initial cancer	**38**	**14.80**	**2.6**[b]	**76**	**27.33**	**2.8**[b]	**43**	**13.29**	**3.2**[b]	**12**	**10.70**	**1.1**	**169**	**66.06**	**2.6**[b]
Buccal cavity, pharynx	**7**	**0.85**	**8.3**[b]	**18**	**1.49**	**12.1**[b]	**8**	**0.67**	**12.0**[b]	**1**	**0.50**	**2.0**	**34**	**3.50**	**9.7**[b]
Lip	0	0.15	0.0	1	0.25	3.9	0	0.11	0.0	0	0.08	0.0	1	0.60	1.7
Tongue	4	0.17	23.5[b]	4	0.30	13.2[b]	4	0.13	30.1[b]	0	0.10	0.0	12	0.70	17.1[b]
Salivary gland	0	0.04	0.0	0	0.07	0.0	0	0.03	0.0	0	0.03	0.0	0	0.17	0.0
Gum, other mouth	2	0.24	8.5	6	0.42	14.3[b]	1	0.19	5.3	1	0.15	6.9	10	0.99	10.1[b]
Pharynx	0	0.22	0.0	7	0.38	18.3[b]	2	0.17	11.8[b]	0	0.13	0.0	9	0.90	10.0[b]
Digestive system	**15**	**4.86**	**3.1**[b]	**26**	**8.80**	**3.0**[b]	**15**	**4.24**	**3.5**[b]	**3**	**3.33**	**0.9**	**59**	**21.22**	**2.8**[b]
Esophagus	7	0.35	20.0[b]	11	0.62	17.7[b]	4	0.28	14.1[b]	1	0.21	4.8	23	1.46	15.7[b]
Stomach	0	0.94	0.0	4	1.61	2.5	2	0.75	2.7	0	0.54	0.0	6	3.83	1.6
Colon	4	1.72	2.3	5	3.21	1.6	4	1.60	2.5	2	1.31	1.5	15	7.83	1.9[b]
Rectum	1	1.03	1.0	4	1.86	2.2	1	0.89	1.1	0	0.69	0.0	6	4.47	1.3
Liver, biliary	1	0.25	4.1	1	0.45	2.2	2	0.22	9.2[b]	0	0.17	0.0	4	1.08	3.7
Pancreas	2	0.49	4.1	1	0.91	1.1	2	0.44	4.5	0	0.35	0.0	5	2.18	2.3
Respiratory system	**5**	**3.13**	**1.6**	**27**	**5.90**	**4.6**[b]	**13**	**2.79**	**4.7**[b]	**3**	**2.25**	**1.3**	**48**	**14.06**	**3.4**[b]
Nasal cavities, sinuses	0	0.03	0.0	1	0.06	16.6	0	0.03	0.0	0	0.02	0.0	1	0.14	6.9
Larynx	0	0.38	0.0	7	0.69	10.1[b]	2	0.31	6.4	2	0.24	8.3	11	1.63	6.8[b]
Trachea, bronchus, lung	5	2.69	1.9	19	5.10	3.7[b]	11	2.43	4.5[b]	1	1.97	0.5	36	12.17	3.0[b]
Prostate gland	4	2.45	1.6	6	4.65	1.3	5	2.46	2.0	2	2.10	1.0	17	11.66	1.5
Testis	0	0.03	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.12	0.0
Kidney, renal pelvis, ureter	1	0.39	2.6	1	0.72	1.4	0	0.34	0.0	1	0.27	3.7	3	1.72	1.7
Bladder, other urinary	2	1.05	1.9	0	1.96	0.0	1	0.98	1.0	0	0.81	0.0	3	4.79	0.6
Melanoma of the skin	0	0.17	0.0	0	0.33	0.0	0	0.15	0.0	0	0.12	0.0	0	0.78	0.0
Eye	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.10	0.0
Brain, central nervous system	0	0.18	0.0	0	0.32	0.0	0	0.14	0.0	0	0.11	0.0	0	0.74	0.0
Thyroid gland	0	0.05	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.19	0.0
Bone	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.10	0.0
Connective tissue	0	0.08	0.0	1	0.14	7.3	0	0.06	0.0	1	0.05	19.4	2	0.33	6.1
Lymphatic, hematopoietic system	**2**	**0.99**	**2.0**	**3**	**1.82**	**1.6**	**2**	**0.88**	**2.3**	**1**	**0.72**	**1.4**	**8**	**4.40**	**1.8**
Non-Hodgkin's lymphoma	1	0.33	3.0	1	0.61	1.6	1	0.29	3.5	1	0.23	4.3	4	1.46	2.7
Hodgkin's disease	0	0.08	0.0	0	0.14	0.0	0	0.06	0.0	0	0.05	0.0	0	0.33	0.0
Multiple myeloma	0	0.14	0.0	0	0.27	0.0	0	0.14	0.0	0	0.11	0.0	0	0.66	0.0
Leukemias	1	0.43	2.3	2	0.80	2.5	1	0.40	2.5	0	0.32	0.0	4	1.95	2.0
Chronic lymphocytic	1	0.14	7.3	1	0.26	3.9	0	0.13	0.0	0	0.11	0.0	2	0.63	3.2
Acute nonlymphocytic	0	0.12	0.0	1	0.23	4.3	0	0.12	0.0	0	0.10	0.0	1	0.57	1.8

[a] ICD-O codes = 146–148.
[b] $P < .05$.

PHARYNX
FEMALES

TABLE 5E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pharynx among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	539			337			116			49			539		
Person-yr in interval	354			747			373			283			1,757		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**5**	**2.77**	**1.8**	**14**	**6.26**	**2.2**[b]	**5**	**3.61**	**1.4**	**6**	**2.80**	**2.1**	**30**	**15.44**	**1.9**[b]
All excluding site of initial cancer	**5**	**2.76**	**1.8**	**14**	**6.23**	**2.2**[b]	**4**	**3.59**	**1.1**	**5**	**2.79**	**1.8**	**28**	**15.37**	**1.8**[b]
Buccal cavity, pharynx	**1**	**0.05**	**18.3**	**1**	**0.12**	**8.2**	**2**	**0.07**	**30.4**[b]	**3**	**0.05**	**61.4**[b]	**7**	**0.29**	**24.0**[b]
Lip	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Tongue	0	0.01	0.0	0	0.03	0.0	0	0.01	0.0	1	0.01	100.8[b]	1	0.06	16.8
Salivary gland	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Gum, other mouth	1	0.02	54.4	1	0.04	23.9	1	0.02	44.3	1	0.02	55.7	4	0.10	39.7[b]
Pharynx	0	0.01	0.0	0	0.03	0.0	1	0.02	66.4	1	0.01	93.3[b]	2	0.07	28.5[b]
Digestive system	**1**	**0.76**	**1.3**	**5**	**1.75**	**2.9**	**0**	**1.12**	**0.0**	**0**	**0.88**	**0.0**	**6**	**4.50**	**1.3**
Esophagus	1	0.02	52.4	1	0.04	22.6	0	0.03	0.0	0	0.02	0.0	2	0.11	18.4[b]
Stomach	0	0.09	0.0	1	0.22	4.6	0	0.14	0.0	0	0.10	0.0	1	0.55	1.8
Colon	0	0.35	0.0	1	0.81	1.2	0	0.53	0.0	0	0.43	0.0	1	2.12	0.5
Rectum	0	0.15	0.0	1	0.35	2.9	0	0.21	0.0	0	0.17	0.0	1	0.88	1.1
Liver, biliary	0	0.05	0.0	1	0.11	8.7	0	0.07	0.0	0	0.06	0.0	1	0.29	3.4
Pancreas	0	0.08	0.0	0	0.18	0.0	0	0.11	0.0	0	0.09	0.0	0	0.46	0.0
Respiratory system	**0**	**0.20**	**0.0**	**2**	**0.46**	**4.4**	**1**	**0.25**	**4.0**	**1**	**0.20**	**5.0**	**4**	**1.10**	**3.6**
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.03	0.0
Larynx	0	0.01	0.0	1	0.03	35.7	1	0.01	71.6	0	0.01	0.0	2	0.07	30.7[b]
Trachea, bronchus, lung	0	0.18	0.0	1	0.41	2.4	0	0.23	0.0	1	0.18	5.5	2	1.00	2.0
Female breast	3	0.77	3.9	2	1.69	1.2	2	0.91	2.2	0	0.71	0.0	7	4.08	1.7
Female genital tract	**0**	**0.50**	**0.0**	**1**	**1.09**	**0.9**	**0**	**0.57**	**0.0**	**0**	**0.41**	**0.0**	**1**	**2.56**	**0.4**
Cervix uteri	0	0.10	0.0	0	0.20	0.0	0	0.10	0.0	0	0.07	0.0	0	0.46	0.0
Corpus uteri	0	0.21	0.0	1	0.48	2.1	0	0.25	0.0	0	0.18	0.0	1	1.13	0.9
Uterus, NOS	0	0.03	0.0	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.15	0.0
Ovary, fallopian tubes	0	0.13	0.0	0	0.29	0.0	0	0.15	0.0	0	0.11	0.0	0	0.69	0.0
Kidney, renal pelvis, ureter	0	0.04	0.0	1	0.10	10.3	0	0.06	0.0	0	0.05	0.0	1	0.25	4.1
Bladder, other urinary	0	0.07	0.0	1	0.16	6.2	0	0.10	0.0	0	0.09	0.0	1	0.42	2.4
Melanoma of the skin	0	0.04	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.19	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.03	0.0
Brain, central nervous system	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.03	0.0	0	0.17	0.0
Thyroid gland	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Bone	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.02	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Lymphatic, hematopoietic system	**0**	**0.17**	**0.0**	**1**	**0.39**	**2.6**	**0**	**0.24**	**0.0**	**0**	**0.19**	**0.0**	**1**	**0.98**	**1.0**
Non-Hodgkin's lymphoma	0	0.07	0.0	0	0.15	0.0	0	0.09	0.0	0	0.07	0.0	0	0.39	0.0
Hodgkin's disease	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.07	0.0
Multiple myeloma	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.17	0.0
Leukemias	0	0.06	0.0	1	0.13	7.5	0	0.09	0.0	0	0.07	0.0	1	0.35	2.9
Chronic lymphocytic	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.10	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.12	0.0

[a] ICD-O codes = 146–148.

[b] $P < .05$.

Second Cancer Following Cancer of the Digestive System in Connecticut, 1935–82 [1]

Shelia K. Hoar,[2] Jerome Wilson,[3] William J. Blot,[4] Joseph K. McLaughlin,[4]
Deborah M. Winn,[2] *and* Arlene F. Kantor[2]

ABSTRACT—The risk of developing a second primary cancer was evaluated in approximately 64,000 persons diagnosed with cancer of the digestive system in Connecticut during 1935–82. Significant excesses of all second cancers combined were observed following cancer of the esophagus (58 observed vs. 33 expected), small intestine (41 vs. 24), and colon (2,268 vs. 1,714). A slight excess of multiple primaries was observed following cancer of the liver and biliary tract (47 vs. 40). The observed number of second cancers was nearly equal to the expected number for persons initially diagnosed with cancers of the stomach (251 vs. 258), rectum (952 vs. 941), and pancreas (40 vs. 40). Persons with initial cancers of the small intestine, colon, and rectum also had excess second cancers arising primarily in the colon, which suggested the influence of common etiologic factors or possibly misclassified metastases in some. Shared dietary, socioeconomic, or hormonal factors may explain the excess of uterine and ovarian cancers among patients with colon cancer and the excess of breast cancer among patients with colon and rectal cancers. Oral and respiratory cancers occurred more frequently than expected in persons with an initial esophageal cancer, which is likely due to common risk factors of cigarette smoking or alcohol intake, or both. The elevations in cancer of the prostate among males with cancers of the esophagus, small intestine, colon, rectum, liver/biliary, and pancreas are probably artifacts associated with increased medical surveillance of cancer patients. The prostate cancer excesses were limited to the first year after diagnosis of the initial cancer or decreased over time for all but cancer of the colon and small intestines. Increased medical surveillance may also contribute to the excess renal and bladder cancers seen within 5 years of diagnosis of stomach cancer. Excesses were also seen for second pancreatic cancer among small intestine and liver/biliary cancer patients and second kidney and brain cancers among those with colon cancer. The deficits of stomach and rectal cancer among persons initially diagnosed with the same tumors, respectively, were anticipated because surgical removal of the organ is the primary form of treatment. Patients with rectal cancer also had deficits of stomach and pancreatic cancers. Future research should clarify the role of diet, alcohol, metabolic and endocrine factors, and host susceptibility on the risk of second neoplasms following cancer of the digestive system.—Natl Cancer Inst Monogr 68: 49–82, 1985.

ESOPHAGUS (ICD-O, 150)

Esophageal cancer accounted for approximately 9,000 cases, or 1%, of all new cancers in the United States in 1983 (*1, 2*). Survival after diagnosis is poor, and the relative 5-year survival rate is only 4% (*3*). Less than 25% of the esophageal cancer patients survive more than 1 year (*4*). The major risk factors for esophageal cancer are cigarette smoking and alcohol intake, especially spirits (*1, 5, 6*). Dietary deficiencies also appear to be involved including low fruit and vegetable consumption, Plummer-Vinson syndrome, zinc deficiency, and poor nutrition in general (*1*). Drinking hot beverages, betel chewing, ionizing radiation, and asbestos exposure may contribute also in some cases. The incidence of esophageal cancer is higher among blacks than whites in the United States, particularly in urban black males (*6–9*).

Despite greatly reduced life expectancy, patients with esophageal cancer are prone to subsequent cancers of several other sites. A previous survey of 1,828 patients with esophageal cancer in Connecticut indicated an excess of second cancers of the mouth (*10*), which is consistent with the tendency of certain individuals to develop multiple carcinomas of the head and neck region (*11*).

Results

In Connecticut, 3,156 persons developed esophageal cancer between 1935 and 1982. Among men, the average age at diagnosis was 64 years, and the average year of diagnosis was 1964, whereas the average age was 65 years and the average year was 1967 for women. The poor survival experience of patients with esophageal cancer was reflected by an average follow-up of only 0.7 year for men and 1.1 years for women. Most of the patients, 61%, received radiation treatment.

Overall, 58 (or 1.8%) of the esophageal cancer patients developed a second primary, compared with 32.6 expected based on rates in the general Connecticut population (RR = 1.78; 95% CI = 1.35–2.30). Men experienced a higher second cancer risk than women, 1.9 and 1.4, respectively. Among men, the excess cancer risk was attributable to new primaries of the buccal cavity, respiratory tract, and

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ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval; SEER = Surveillance, Epidemiology, and End Results (Program); NOS = not otherwise specified.

[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Environmental Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 4C16, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Shelia K. Hoar, Sc.D.

[3] Radiation Epidemiology Branch, Division of Cancer Etiology.

[4] Biostatistics Branch, Division of Cancer Etiology.

prostate gland. An increased risk for cancer of the buccal cavity and pharynx (RR = 4.8; 95% CI = 1.7–10.4) was based on cancers distributed over various subsites, including the lip, tongue, and gum/floor of the mouth. In males, lung cancer primaries occurred 2.3 times more often in patients with esophageal cancer than expected ($n = 10$). A 3.5-fold increased incidence was observed of new primaries of the prostate, which accounted for 49% of the excess second cancers in patients with esophageal cancer. Fourteen of the 15 prostate cancers were diagnosed in the first 4 years of follow-up.

Among women, 5 of the 12 second primaries occurred in the buccal cavity and pharynx, in comparison to 0.2 expected (95% CI = 11–78). Included were 3 tongue cancers (0.03 expected) and 2 cancers of the gum or floor of the mouth (0.1 expected). In both sexes, the observed number of second cancers in the digestive system equaled the expected number. Only 1 second esophageal cancer was reported; no significant deficit of any second tumor occurred.

Discussion

Despite a typically poor survival experience, patients with esophageal cancer had second cancers significantly more often than expected. The 1.8-fold increased risk was attributable to excesses of oral cancer in both sexes and respiratory and prostate cancers among men. This pattern is consistent with previous observations (*11, 12*).

The relationship of esophageal cancer to oral cavity and respiratory cancers has been reported several times (*10–17*) and suggests a common etiology. Tobacco smoking can be linked to the association with lung cancer, and smoking and alcohol intake is linked to oral, pharyngeal, laryngeal, and secondary esophageal cancers. About as many women as men developed cancer of the buccal cavity and pharynx subsequent to esophageal cancer; thus a male-to-female ratio much lower than is typical was observed for oral and pharyngeal cancers (*5*).

Not only were patients with an esophageal cancer more likely to develop cancers of the buccal cavity or larynx, but an excess of esophageal cancer subsequent to buccal and laryngeal cancers was also seen in Connecticut (*18, 19*). However, in contrast to the significant excess of lung cancer occurring after esophageal cancer in men, no excess of esophageal cancer after lung cancer was found (*10, 19*). The most common second cancer recorded among men was that of the prostate gland. Blacks in the United States are at high risk of esophageal (*5*) and prostatic cancers (*20*). However, the excess prostate cancer was probably due to increased medical surveillance after the initial primary, inasmuch as 14 of the 15 prostate tumors were detected within the first 4 years after diagnosis of the initial cancer. The rate of other second primary cancers did not decline over time since diagnosis. This finding suggests that either 1) esophageal cancer patients do not change their smoking and drinking patterns subsequent to the diagnosis of cancer, or 2) there is no reduction in risk for at least 10 years for a second cancer associated with the risk factors for an initial esophageal cancer.

STOMACH (ICD-O, 151)

The incidence and mortality rates for stomach cancer have been steadily declining in the United States. Once the most common cancer, in 1983 it accounted for about 3% of all cancers and was ranked ninth in numbers of new cases and sixth in numbers of deaths (*2*). Although dietary and nutritional factors are strongly suspect, causes of stomach cancer and the reasons for its decline remain unclear (*21*). The cancer is generally fatal. Most patients die within 1 year of diagnosis, and the 5-year relative survival rate has been estimated to be about 13%. Among 12,835 patients reported to the SEER Program between 1973 and 1980 (*22*), initial treatment was surgery only (41%), chemotherapy without radiotherapy (22%), radiotherapy without chemotherapy (5%), and other treatments or none (32%).

Results

Of the 10,248 persons who developed stomach cancer in Connecticut during 1935–82, 63% of the cancers occurred among males. A total of 251 second primary tumors were reported, compared with 258 expected based on general population rates (RR = 0.97; 95% CI = 0.86–1.10). The distribution of these second tumors was about as expected, except for an increased number of urinary tract tumors. Males had 11 kidney/ureter cancers and 21 bladder and other urinary cancers, significantly more than the expected numbers of 4.1 and 12.5, respectively. The corresponding RR were 2.7 (95% CI = 1.3–4.8) and 1.7 (95% CI = 1.0–2.6). All the excess renal cancer and much of the excess bladder cancer occurred within 5 years of diagnosis. No increases in kidney or bladder cancers were seen among females with stomach cancer. No cancers occurred significantly less often than expected, except for second stomach cancers ($n = 2$, RR = 0.1).

Discussion

Little evidence was found that persons with stomach cancer experienced any increased risk of subsequent cancers. Although an excess of urinary tract cancers were reported among these patients, the increase was limited to males and was largely confined to second tumors diagnosed within a few years of the initial cancer. Stomach cancer was not excessive among patients with kidney or bladder cancers in the earlier Connecticut survey (*10*). The deficit of second stomach cancers was anticipated because surgical removal of the stomach is the primary form of treatment for this cancer. The results are consistent with the earlier survey, when 107 cancers occurred subsequent to stomach cancer, whereas 118 were expected (*10*).

SMALL INTESTINE (ICD-O, 152)

In 1983, cancer of the small intestine accounted for approximately 2,100 cases or 0.2% of all cancers diagnosed in the United States (*2*). Although the small intestine comprises about 75% of the length and 90% of the surface area of the gastrointestinal tract, cancers of the small intestine account for only 1% of all gastrointestinal cancers. Different risk factors appear to be associated with the 4 major histologic types of stomach neoplasms (*23*). Adenocarcinomas are the most common type and are occasionally associated with regional enteritis (Crohn's disease), Peutz-Jeghers syndrome, familial polyposis coli, and Gardner's syndrome. Lymphomas of the small intestine (grouped with other non-Hodgkin's lymphomas in this survey) are occasionally seen with immune deficiency states and celiac disease and occur excessively in the Middle East. Little is known about the etiology of carcinoid tumors and leiomyosarcoma. The 5-year survival rate in a Saskatchewan case series was 23% for noncarcinoid cancers of the small intestine and 64% for malignant carcinoids (*24*).

Multicentric and multiple primary cancers have been associated with both carcinoid and noncarcinoid tumors of the small intestine (*10, 24-27*). In the Connecticut survey from 1935 to 1964, the increase was twofold in subsequent primary cancer for both men and women, especially for cancers of the liver/biliary, pancreas, and ovary (*10*). Colorectal carcinoma has been seen most often following a carcinoid tumor of the small intestine (*27, 28*).

Results

At diagnosis, the average age was 60 years and the average year was 1966 for the 554 persons in Connecticut who developed cancer of the small intestine between 1935 and 1982. The average length of follow-up was 3.8 years. Less than 4% of the patients initially received radiation treatment. Overall, 41 (or 7%) of the patients with cancer of the small intestine developed a second tumor, compared with 23.6 cases expected based on rates in the general population (RR = 1.74; 95% CI = 1.25-2.35). The risk of developing a second cancer was higher in men (2.0) than in women (1.4). Among men, the excess of second tumors varied little according to time since diagnosis of the initial cancer. However, among women, the excess was greatest during the first year after the initial cancer with no excess seen after 5 years.

Cancers of the digestive organs accounted for 42% of all second tumors and 56% of the excess second tumors observed (RR = 2.3; 95% CI = 1.4-3.8). The excess was largely due to increased rates of colon cancer. Six of the 7 second colon cancers were adenocarcinomas and 1 was classified as a carcinoma, NOS, of the cecum. Similarly, 6 of the 7 primary cancers of the small intestine were adenocarcinomas and 1 was classified as a malignant carcinoid. In both sexes combined, the risk of colon cancer appeared to increase with time since diagnosis of the first cancer. Although based on small numbers, cancers of the rectum and pancreas also occurred excessively among men. Within 1 year of the first cancer, 2 women were diagnosed with a hepatobiliary (1 liver and 1 gallbladder) cancer with 0.03 expected. Seven cases of prostate cancer were diagnosed among the men; 2.3 were expected. No statistically significant deficit of any second tumor was seen.

Discussion

The small intestine might be expected to be a frequent site of cancer because its cells undergo constant proliferation, and it lies between the stomach and the large intestine, which are common cancer sites in various parts of the world (*23*). However, the small intestine is a rare tumor site and several explanations have been advanced, including the relative absence of bacterial flora as compared with the large intestine (*29, 30*). Lowenfels (*29*) has hypothesized that protective immune mechanisms may exist in the small intestine and their impairment might result in neoplasms of the small intestine and other sites.

In our survey, patients with cancer of the small intestine had a significant 74% increased risk of developing a second cancer. Although based on small numbers, most of the excess risk was due to cancer of the digestive organs including the colon and pancreas, which indicates the possibility of shared nutritional or other factors. This is consistent with international studies that demonstrate a strong correlation between incidence rates for cancers of the small and large intestine (*29*). Cancer of the prostate accounted for 27% of the excess second cancers in our survey, which is probably due to increased medical surveillance of cancer patients, although the excess persisted over time since diagnosis of the first cancer. Risks were not significantly increased for lymphoma or melanoma, as found in certain immunocompromised populations, so that defective immunity would not explain the predisposition to certain tumors among patients with small intestinal cancer.

COLON (ICD-O, 153)

Colon cancer is second only to that of lung as the most common cause of cancer death in the United States. It accounts for approximately 48,600 (or 11%) of all cancer deaths per year and 85,000 (or 10%) of all new cancers (*2*). Data from the First (1937-39), Second (1947-48), and Third (1969-71) National Cancer Surveys showed increasing incidence rates of colon cancer among white and nonwhite males. Incidence rates among white females rose and stabilized (*31*). Colon cancer incidence also increased in both men and women in Connecticut from 1935 to 1960 and then leveled off (*32*). Mortality rates for colon cancer in the United States from 1935 to the present have increased in every race-sex group except among white females (*31*). The 5-year survival rate has changed only slightly from 42 to 47% for men over the period 1960-63 to 1970-73 and from 44 to 50% for women over the same period (*3*). Incidence rates vary widely around the world and within countries (*32*). In the United States, colon cancer is more common in the North than in the South, in urban areas, in higher socioeconomic classes, and in certain ethnic groups (*33-36*).

The central role of environmental factors is indicated by studies showing that persons migrating from low to high-risk areas gradually assume the risk prevalent in the new area (*32, 37*). Dietary habits appear to be important, such as high fat and low fiber diets. A familial tendency to colon cancer exists with or without a polyposis syndrome. Only limited evidence is available to implicate occupational exposures such as asbestos, acrylonitrile, yarn, and textiles (*32, 38, 39*). Some colon cancers complicate inflammatory diseases, especially ulcerative colitis.

In earlier surveys of multiple primary tumors, patients with colon cancer showed a significant increased risk for cancers of the colon, rectum, small intestine, corpus uteri, ovary, prostate, and lymphoma (*10, 40, 41*). Two hospital series of patients with colorectal cancer indicated 50–70% excesses of second cancers (*40, 42*). No excess of second tumors was found in a follow-up of patients treated in Veterans Administration clinical trials for colorectal cancer (*43*).

Results

Between 1935 and 1982, a total of 26,804 persons developed colon cancer in Connecticut. The average year of diagnosis was 1966, and the average age at diagnosis was 66 years. The average follow-up was 4.5 years. Overall, 2,268 (or 8%) of the colon cancer patients developed a second cancer compared with 1,714 expected (RR = 1.32; 95% CI = 1.27–1.38). When second cancers of the colon are excluded, this estimate was lowered slightly (RR = 1.2; 95% CI = 1.1–1.3). The risk of developing a second cancer was the same for both sexes. A significant excess of second primary cancers persisted for 30 years with risk increasing over time, up to 1.7. Risk of developing a second cancer was higher in young patients than older patients. The RR by age less than 45 years, 45 to 54 years, and over 55 years at first diagnosis were 2.9, 1.7, and 1.2 for all second cancers, and 8.7, 3.7, and 1.8 for second colon cancers.

Cancers of the digestive tract accounted for 69% of the excess risk among colon cancer patients. Among both sexes, 506 second colon cancer cases were diagnosed compared with 245.4 expected (RR = 2.1; 95% CI = 1.9–2.3). The excess colon cancer risk increased with time since diagnosis of the initial cancer. Rectal cancer risk was also elevated approximately twofold (RR = 1.9; 95% CI = 1.6–2.2).

Significant excesses of second cancers occurred in the female reproductive organs. Overall, breast cancer risk was elevated 20% with the excess limited to women observed 10 or more years (RR = 1.5; 95% CI = 1.2–1.9). Cancer of the uterine corpus was significantly increased 1.7-fold overall (95% CI = 1.4–2.1), with the largest risks appearing after 10 or more years (RR = 2.3; 95% CI = 1.5–3.3). The relationship with latency was not altered when the uterine corpus cancers were combined with cancers of the uterus, NOS. The excess risk for ovarian cancer (RR = 2.4; 95% CI = 1.9–3.0) dissipated after 5 years of observation. Significant excesses were also observed for cancers of the prostate (RR = 1.3; 95% CI = 1.2–1.5) and kidney (RR = 1.4; 95% CI = 1.0–1.9).

Brain cancer was elevated in both sexes, but statistically significant in women only. Nonsignificant excesses with RR greater than 1.3 based on at least 10 observed cases were seen for the following: melanoma in both sexes; cancers of the tongue, pharynx, and liver/biliary, and acute nonlymphocytic leukemia among men; and esophageal cancer among women. No cancer sites occurred significantly below expectation. In contrast to many cancers, cancer of the colon was not followed by an excess of lung tumors (RR = 0.9; 95% CI = 0.8–1.0). Only 2% of the patients were treated initially with radiation, but among irradiated women, a significant excess of bladder cancer was observed ($n = 2$; RR = 14.6).

Discussion

Colon cancer, a common tumor, shows an adequate survival rate, with which we can assess the risk of patients developing a second primary cancer. Overall, the risk of multiple cancers was increased 1.3-fold with significant excesses seen for second cancers of the colon and rectum in both sexes, cancers of the breast, corpus uteri, ovary, and brain among women, and cancers of the prostate, kidney, and thyroid among men.

Many of these multiple primary complexes may be related to shared environmental or host factors (*32, 44*). An increased risk of colon and rectal cancer following colon cancer was anticipated because these sites share exposures and susceptibility states, and a tendency to multifocal carcinoma of the colon and rectum has been previously reported (*13, 40, 45*). Although exclusion of misdiagnosed metastatic disease is not possible in some cases, this problem appears to be minimal because the risk of second cancer of the large bowel was not significantly elevated until 5 years after the first primary.

The association of colon cancer with cancers of the breast, corpus uteri, and ovary has been reported in several studies (*40, 45*), including the earlier report of the Connecticut experience during 1935–64 (*27*). The risks persisted in the present analysis which extended the observation period through 1982. The mechanism underlying this array of tumors is not clear, but dietary and hormonal factors may play a role. Genetic factors may also be occasionally involved, inasmuch as the same constellation of tumors had been reported in familial adenocarcinomatosis (*46*).

Because 51% of the cases developed during 4 years following diagnosis of the first primary, the excess of prostate cancer may be related to increased medical surveillance. However, a significant RR of 1.3 was still present after 10 years of follow-up, which suggests a shared etiologic factor. The kidney cancer excess, which rose with increasing follow-up, remains unexplained. Cigarette smoking, the only established risk factor for kidney cancer (*47–50*), is not related to colon cancer, but similar dietary factors such as fat consumption may be involved (*32, 51*). A significant risk of developing brain cancer, especially among women, is interesting in view of the association between hereditary polyposis and brain tumors in Turcot's syndrome (*52*). The excess of thyroid cancer in males is also noteworthy because of reports of this tumor with the form of polyposis called Gardner's syndrome (*53*). No excess of lymphoma was observed, in contrast to a previous report of synchronous multiple tumors (*41*).

Treatment for colon cancer did not appear to influence greatly subsequent cancer risk. Radiation treatment may account for the 2 excess bladder cancers observed among the irradiated women. Although leukemia appears to be a late consequence of chemotherapy with nitrosoureas for gastrointestinal cancer (*54, 55*), the absence of a significant risk in our study is consistent with findings from the SEER Program (*22*) and perhaps reflects the low frequency of this type of therapy among patients with colon cancer.

Although this survey showed that the risk of several cancers was significantly elevated following colon cancer, some associations may be due to chance given the number of sites examined. Moreover, the separate analysis of colon and rectal cancers may have introduced classification error. This might vary over time, particularly because the data were collected over 47 years during which diagnostic practices and techniques have changed.

RECTUM (ICD-O, 154)

In 1983, cancer of the rectum accounted for approximately 39,000 (or 5%) of all cancers diagnosed in the United States and 19% of all gastrointestinal cancers (*2*). The incidence rates for rectal and colon cancers are highly correlated, and it is likely that major risk factors for these tumors are shared. However, the origins are not entirely the same, as suggested by the higher male-to-female ratio for rectal cancer. Recent studies have also suggested an association with beer drinking among persons with rectal cancer, although the findings are not conclusive (*32, 34, 56, 57*).

Data from the Second (1947–48) and the Third (1969–71) National Cancer Surveys showed a decrease over time in the incidence of rectal cancer in every race–sex group except nonwhite men (*31*). Rectal cancer incidence appeared nearly stable in Connecticut from 1940 to the present, but a slight increase was seen in men over age 65 (*32*). Mortality from rectal cancer in the United States has decreased since 1950 (*31*). The 5-year survival rate is 34% for white men, 38% for white women, 22% for black men, and 34% for black women (*58*).

In the earlier Connecticut survey, patients with rectal cancer showed no increased risk overall for subsequent primary tumors, although significant excesses were noted for cancers of the colon, ovary, and prostate (*10*). A study of rectal cancer cases from the Memorial Sloan-Kettering Cancer Center indicated significant excess cancers of the kidney, bladder, and skin, and nonsignificant excesses of cancers of the breast and oral cavity (*40*).

Results

Between 1935 and 1982, the average age at diagnosis was 65 years for the 15,460 persons in Connecticut who developed cancer of the rectum, rectosigmoid junction, and anus (hereafter referred to as "rectum"). The average year of diagnosis was 1964, and the average length of follow-up was 4.4 years. Ten percent of the patients initially received radiation treatment.

Overall, 952 (or 6%) of the rectal cancer cases developed a second tumor compared with 941 expected (RR = 1.01; 95% CI = 0.95–1.08). The risk of developing a second cancer did not differ by sex. However, 10 years after the diagnosis of rectal cancer, a slight excess risk of second cancers was observed (1.2; 95% CI = 1.0–1.3). Among the 231 persons with cancer of the anus, 11 second cancers developed, whereas 15.4 were expected.

Elevations in risk were observed for cancers of the colon (RR = 1.7; 95% CI = 1.5–2.0) and the prostate (RR = 1.3; 95% CI = 1.1–1.5). The RR for colon cancer increased with time since diagnosis of the initial cancer, from 1.3–1.5 to 2.2 (95% CI = 1.8–2.8) after 10 years of follow-up. However, the RR for prostate cancer decreased over time and reached unity 10 years after diagnosis of the initial cancer. A significant excess of breast cancer was seen among women 10 years after diagnosis of rectal cancer (RR = 1.6; 95% CI = 1.1–2.2). Nonsignificant excesses of multiple myeloma and ovarian cancer were observed. Cancers of the stomach, pancreas, and rectum occurred significantly less frequent than expected.

Discussion

No overall excess of second primary tumors following cancer of the rectum were noted, but significant excesses were observed for cancers of the colon and prostate. The colon cancer excess, which increased over time, is consistent with the reported tendency of patients with large bowel cancer to develop multifocal tumors of the colon and rectum (*32, 34*). When cancers of the rectum and colon are excluded, the risk of other second cancers was slightly lower than expected (0.94; 95% CI = 0.87–1.0). The prostate cancer excess decreased with time, which suggests the influence of medical surveillance among cancer patients. Breast cancer was observed in excess in 10-year survivors; this finding is consistent with previous reports linking this tumor with colon and rectal cancer (*40, 59–61*).

No excess of cervical or uterine cancer was observed among rectal cancer patients in contrast to an increased risk of rectal cancer reported among women with these gynecologic tumors (*59, 60, 62*), probably due to radiation treatment rather than common etiologic factors (*60, 62*). Deficits of stomach, pancreatic, and rectal cancers were observed. Surgical removal of the rectum at initial diagnosis removes the risk of subsequent rectal cancer, but reasons for the decreased risk of stomach and pancreatic cancers are unclear.

LIVER, GALLBLADDER, AND OTHER BILIARY CANCER (ICD-O, 155-156)

Liver, gallbladder, and other biliary cancers together accounted for less than 2% of all cancers in the United States in 1983 (*2*). Almost 60% of the cancers in this category are derived from the biliary tract (*7*). The major risk factors for primary liver cancer include infection with hepatitis B virus and alcohol consumption (*63*), whereas those for the biliary tract include gallstones and associated aspects of diet and hormonal status (*64*). The survival rates associated with these 2 cancers are equally poor and have not appreciably improved over time (*3*). The 5-year relative survival rate for liver cancer is 2% for males and 6% for females, and for biliary tract cancer it is 7% for males and 9% for females (*3*). Approximately 50% of the patients with liver cancer and 40% of those with biliary cancer have metastatic disease at the time of initial diagnosis (*4*). A previous survey of the Connecticut experience revealed an increased risk of second cancers among males, especially for prostate and kidney cancers (*10*).

Results

Among the 2,745 persons with liver, gallbladder, and other biliary cancer, 47 (or 2%) developed a second tumor. The average age at diagnosis of the first cancer was 66 years and the average year of diagnosis was 1965. Follow-up averaged 1.2 years. Few patients, only 9%, received initial radiation treatment. Of the 47 second cancers, 41 (or 87%) occurred in biliary cancer patients, so the results presented apply mainly to this tumor. When possible, separate risk estimates are presented for liver and biliary tract cancers.

The overall risk of developing a second primary cancer was not significantly increased following hepatobiliary cancer (1.18; 95% CI = 0.87–1.56). However, the risk was higher among males (RR = 1.4) than females (1.0). A significantly elevated risk was seen for second cancers of the pancreas (RR = 5.3). Six of the 7 patients with pancreatic cancer had biliary tract cancer as their first diagnosis. A significantly elevated risk of rectal cancer was observed among females (RR = 3.9). All 5 of these second primary cancers involved patients whose first diagnosis was biliary tract cancer (RR = 4.3; 95% CI = 1.4–10.0) and occurred between the first and fourth years of observation. There were no cases of rectal cancer among the males. The risk of prostate cancer was elevated (RR = 2.2) but not significantly; 3 of the 8 second primaries occurred in patients with an initial liver cancer, whereas 0.6 were expected. No second primary cancers occurred significantly below expectation. Only 75 (or 3%) patients were alive 10 years after diagnosis and they developed 6 second tumors (RR = 0.8).

Discussion

As a result of poor survival, few patients with hepatobiliary cancer live long enough to develop a second tumor. The overall risk of a second cancer was not significantly elevated. However, the risks for cancer of the pancreas in both sexes and rectal cancer in females were significantly high. Although it has been suggested that bile duct and pancreatic cancers share risk factors (*64*), the excess of the latter type might reflect a misdiagnosis of metastasis from the bile duct to adjacent organs. The excess of rectal cancer following biliary cancer in females is interesting, although in the Connecticut series no excess of hepatobiliary cancer was found among females with rectal cancer (RR = 1.1). Recent studies have suggested that patients (especially women) who have undergone cholecystectomy are prone to large bowel cancer, but the excess risks have involved mainly the proximal rather than distal portions of the large intestine (*65, 66*). The excess risk of prostate cancer among liver cancer patients is probably a result of increased medical surveillance (*67*).

PANCREAS (ICD-O, 157)

In 1983, cancer of the pancreas accounted for about 3% of all newly diagnosed cancers and 5% of all cancer deaths in the United States (*2*). Except for cigarette smoking, few risk factors are known for this disease (*68–70*). Survival after pancreatic cancer is poor and has not improved over time (*3*). The 1- and 5-year relative survival rates are 15% and 2%, respectively (*58*); 61% of the patients have distant metastases at diagnosis (*4*). An earlier survey of multiple primaries from the Connecticut Tumor Registry found no significantly increased risks except for prostate cancer (*10*). Three other sites among males (testis, thyroid, and other respiratory organs) were significantly elevated but were based on only 1 case per site.

Results

Of the 4,972 persons who developed cancer of the pancreas during 1935–82, slightly more men (2,655) than women (2,317) were diagnosed with this disease. The average age at diagnosis was 64 years for men and 67 years for women, and the average year of diagnosis was 1967 for both. The average follow-up was 6 months. About 11% of the patients intitially received radiation treatment, but most received no treatment.

Overall, 40 patients (or <1%) developed a second cancer, which corresponded to the expected number based on rates in the general population (RR = 1.00; 95% CI = 0.72–1.36). Among males, 29 had second tumors, compared with an expected number of 24 (RR = 1.2), and among females, 11 had second primaries with 16 expected (RR = 0.7). Sixteen of the 29 second tumors among males were prostate cancers (RR = 3.5; 95% CI = 2.0–5.7). No site occurred significantly below expectation. Over 50% of the second cancers occurred within a year of diagnosis. Only 33 patients survived for 10 years or more after the initial cancer. Among the 521 patients whose initial primaries were treated with radiation, 7 second cancers occurred in men (RR = 1.4; 95% CI=1.1–5.9) and none in women. Three of the 7 cancers were of the prostate (RR = 7.1; 95% CI = 1.4–25), and 1 was a non-Hodgkin's lymphoma.

Discussion

Due to the extremely poor survival experience of patients with pancreatic cancer, a second primary tumor has little opportunity to develop; overall, the risk was similar to that of the general population. Males did show an excess of prostate cancer, which probably reflected a medical surveillance bias. No excess of lung cancer or other smoking-related sites was observed, despite the association of pancreatic cancer with smoking habits (*69, 70*).

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ESOPHAGUS
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the esophagus, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,450	706	3,156
No. who developed a second primary cancer	46	12	58
Average age at diagnosis of first cancer, yr	64	65	64
Average yr of diagnosis of first cancer	1963	1967	1964
Person-yr of follow-up	1,689	765	2,454
Average follow-up, yr	0.7	1.1	0.8
Percent given radiotherapy for first cancer	60.4	64.2	61.3

[a] ICD-O code = 150.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the esophagus in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	53	91.4
Only the first cancer	2	3.5
Only the second cancer	2	3.5
Neither first nor second cancer	1	1.7
Total second primary cancers	58	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

ESOPHAGUS
BOTH SEXES

TABLE 1C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the esophagus among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,156			766			76			25			3,156		
Person-yr in interval	1,275			831			205			143			2,454		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**30**	**16.08**	**1.9**[b]	**20**	**11.06**	**1.8**[b]	**5**	**2.86**	**1.7**	**3**	**2.60**	**1.2**	**58**	**32.57**	**1.8**[b]
All excluding site of initial cancer	**30**	**15.75**	**1.9**[b]	**19**	**10.86**	**1.7**[b]	**5**	**2.82**	**1.8**	**3**	**2.56**	**1.2**	**57**	**31.96**	**1.8**[b]
Buccal cavity, pharynx	**5**	**0.75**	**6.7**[b]	**4**	**0.46**	**8.6**[b]	**2**	**0.11**	**18.9**[b]	**0**	**0.09**	**0.0**	**11**	**1.41**	**7.8**[b]
Lip	0	0.13	0.0	0	0.07	0.0	1	0.01	69.7	0	0.02	0.0	1	0.24	4.2
Tongue	1	0.15	6.6	3	0.09	31.9[b]	0	0.02	0.0	0	0.02	0.0	4	0.28	14.1[b]
Salivary gland	0	0.04	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Gum, other mouth	3	0.21	14.2[b]	0	0.14	0.0	1	0.03	31.5	0	0.03	0.0	4	0.41	9.9[b]
Pharynx	1	0.18	5.5	1	0.12	8.7	0	0.03	0.0	0	0.02	0.0	2	0.35	5.8
Digestive system	**9**	**5.23**	**1.7**	**2**	**3.53**	**0.6**	**0**	**0.93**	**0.0**	**0**	**0.85**	**0.0**	**11**	**10.53**	**1.0**
Esophagus	0	0.33	0.0	1	0.20	5.0	0	0.04	0.0	0	0.04	0.0	1	0.61	1.6
Stomach	2	0.95	2.1	0	0.59	0.0	0	0.15	0.0	0	0.13	0.0	2	1.82	1.1
Colon	2	1.98	1.0	1	1.40	0.7	0	0.39	0.0	0	0.36	0.0	3	4.12	0.7
Rectum	2	1.07	1.9	0	0.72	0.0	0	0.18	0.0	0	0.16	0.0	2	2.14	0.9
Liver, biliary	2	0.28	7.1	0	0.20	0.0	0	0.05	0.0	0	0.05	0.0	2	0.58	3.4
Pancreas	1	0.53	1.9	0	0.36	0.0	0	0.09	0.0	0	0.09	0.0	1	1.07	0.9
Respiratory system	**2**	**2.82**	**0.7**	**6**	**1.91**	**3.1**[b]	**3**	**0.45**	**6.6**[b]	**2**	**0.36**	**5.5**	**13**	**5.54**	**2.3**[b]
Nasal cavities, sinuses	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Larynx	2	0.32	6.2	1	0.21	4.8	0	0.05	0.0	0	0.03	0.0	3	0.61	4.9
Trachea, bronchus, lung	0	2.44	0.0	5	1.66	3.0	3	0.39	7.6[b]	2	0.32	6.2	10	4.81	2.1
Female breast	1	0.83	1.2	0	0.78	0.0	0	0.26	0.0	0	0.21	0.0	1	2.08	0.5
Female genital tract	**0**	**0.50**	**0.0**	**1**	**0.47**	**2.1**	**0**	**0.15**	**0.0**	**0**	**0.11**	**0.0**	**1**	**1.23**	**0.8**
Cervix uteri	0	0.09	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.21	0.0
Corpus uteri	0	0.21	0.0	0	0.19	0.0	0	0.06	0.0	0	0.05	0.0	0	0.51	0.0
Uterus, NOS	0	0.04	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Ovary, fallopian tubes	0	0.13	0.0	1	0.13	7.9	0	0.04	0.0	0	0.03	0.0	1	0.33	3.0
Prostate gland	9	2.21	4.1[b]	5	1.37	3.6[b]	0	0.31	0.0	1	0.38	2.6	15	4.27	3.5[b]
Testis	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Kidney, renal pelvis, ureter	0	0.37	0.0	0	0.25	0.0	0	0.06	0.0	0	0.05	0.0	0	0.74	0.0
Bladder, other urinary	0	1.00	0.0	2	0.66	3.0	0	0.17	0.0	0	0.17	0.0	2	1.99	1.0
Melanoma of the skin	0	0.17	0.0	0	0.12	0.0	0	0.03	0.0	0	0.03	0.0	0	0.34	0.0
Eye	0	0.02	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.05	0.0
Brain, central nervous system	0	0.17	0.0	0	0.11	0.0	0	0.03	0.0	0	0.02	0.0	0	0.33	0.0
Thyroid gland	2	0.06	35.8[b]	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	2	0.12	17.2[b]
Bone	0	0.03	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.05	0.0
Connective tissue	0	0.08	0.0	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	0	0.15	0.0
Lymphatic, hematopoietic system	**0**	**1.03**	**0.0**	**0**	**0.71**	**0.0**	**0**	**0.18**	**0.0**	**0**	**0.17**	**0.0**	**0**	**2.09**	**0.0**
Non-Hodgkin's lymphoma	0	0.35	0.0	0	0.25	0.0	0	0.06	0.0	0	0.06	0.0	0	0.71	0.0
Hodgkin's disease	0	0.07	0.0	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	0	0.14	0.0
Multiple myeloma	0	0.16	0.0	0	0.11	0.0	0	0.03	0.0	0	0.03	0.0	0	0.33	0.0
Leukemias	0	0.45	0.0	0	0.30	0.0	0	0.08	0.0	0	0.08	0.0	0	0.91	0.0
Chronic lymphocytic	0	0.14	0.0	0	0.10	0.0	0	0.02	0.0	0	0.03	0.0	0	0.29	0.0
Acute nonlymphocytic	0	0.13	0.0	0	0.09	0.0	0	0.02	0.0	0	0.02	0.0	0	0.27	0.0

[a] ICD-O code = 150.

[b] $P < .05$.

ESOPHAGUS
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the esophagus among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,450			554			41			15			2,450		
Person-yr in interval	955			544			111			78			1,689		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**24**	**12.82**	**1.9**^{b}	**15**	**7.91**	**1.9**^{b}	**4**	**1.76**	**2.3**	**3**	**1.72**	**1.7**	**46**	**24.19**	**1.9**^{b}
All excluding site of initial cancer	**24**	**12.52**	**1.9**^{b}	**15**	**7.74**	**1.9**^{b}	**4**	**1.72**	**2.3**	**3**	**1.69**	**1.8**	**46**	**23.64**	**1.9**^{b}
Buccal cavity, pharynx	**3**	**0.69**	**4.3**	**2**	**0.41**	**4.9**	**1**	**0.09**	**11.5**	**0**	**0.08**	**0.0**	**6**	**1.26**	**4.8**^{b}
Lip	0	0.13	0.0	0	0.07	0.0	1	0.01	76.3	0	0.01	0.0	1	0.23	4.4
Tongue	0	0.14	0.0	1	0.08	12.1	0	0.02	0.0	0	0.01	0.0	1	0.25	4.0
Salivary gland	0	0.03	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.06	0.0
Gum, other mouth	2	0.19	10.5^b	0	0.12	0.0	0	0.03	0.0	0	0.02	0.0	2	0.35	5.7
Pharynx	1	0.17	5.9	1	0.10	9.7	0	0.02	0.0	0	0.02	0.0	2	0.31	6.4
Digestive system	**8**	**4.21**	**1.9**	**0**	**2.51**	**0.0**	**0**	**0.54**	**0.0**	**0**	**0.54**	**0.0**	**8**	**7.79**	**1.0**
Esophagus	0	0.30	0.0	0	0.17	0.0	0	0.04	0.0	0	0.03	0.0	0	0.55	0.0
Stomach	2	0.82	2.4	0	0.45	0.0	0	0.09	0.0	0	0.09	0.0	2	1.45	1.4
Colon	2	1.50	1.3	0	0.93	0.0	0	0.21	0.0	0	0.21	0.0	2	2.84	0.7
Rectum	1	0.88	1.1	0	0.53	0.0	0	0.12	0.0	0	0.11	0.0	1	1.63	0.6
Liver, biliary	2	0.21	9.4^b	0	0.13	0.0	0	0.03	0.0	0	0.03	0.0	2	0.40	5.0
Pancreas	1	0.42	2.4	0	0.26	0.0	0	0.05	0.0	0	0.05	0.0	1	0.79	1.3
Respiratory system	**1**	**2.60**	**0.4**	**6**	**1.70**	**3.5**^{b}	**3**	**0.39**	**7.6**^{b}	**2**	**0.30**	**6.6**	**12**	**4.99**	**2.4**^{b}
Nasal cavities, sinuses	0	0.03	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.05	0.0
Larynx	1	0.31	3.2	1	0.19	5.1	0	0.05	0.0	0	0.03	0.0	2	0.58	3.5
Trachea, bronchus, lung	0	2.24	0.0	5	1.47	3.4^b	3	0.34	8.8^b	2	0.27	7.5	10	4.32	2.3^b
Prostate gland	9	2.21	4.1^b	5	1.37	3.6^b	0	0.31	0.0	1	0.38	2.6	15	4.27	3.5^b
Testis	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Kidney, renal pelvis, ureter	0	0.32	0.0	0	0.20	0.0	0	0.05	0.0	0	0.04	0.0	0	0.61	0.0
Bladder, other urinary	0	0.91	0.0	2	0.57	3.5	0	0.13	0.0	0	0.14	0.0	2	1.74	1.2
Melanoma of the skin	0	0.13	0.0	0	0.08	0.0	0	0.02	0.0	0	0.02	0.0	0	0.25	0.0
Eye	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Brain, central nervous system	0	0.14	0.0	0	0.09	0.0	0	0.02	0.0	0	0.01	0.0	0	0.25	0.0
Thyroid gland	1	0.03	29.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	1	0.06	15.7
Bone	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.04	0.0
Connective tissue	0	0.06	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.12	0.0
Lymphatic, hematopoietic system	**0**	**0.82**	**0.0**	**0**	**0.51**	**0.0**	**0**	**0.11**	**0.0**	**0**	**0.11**	**0.0**	**0**	**1.55**	**0.0**
Non-Hodgkin's lymphoma	0	0.27	0.0	0	0.17	0.0	0	0.04	0.0	0	0.03	0.0	0	0.51	0.0
Hodgkin's disease	0	0.06	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.11	0.0
Multiple myeloma	0	0.12	0.0	0	0.08	0.0	0	0.02	0.0	0	0.02	0.0	0	0.24	0.0
Leukemias	0	0.37	0.0	0	0.23	0.0	0	0.05	0.0	0	0.05	0.0	0	0.70	0.0
Chronic lymphocytic	0	0.12	0.0	0	0.07	0.0	0	0.02	0.0	0	0.02	0.0	0	0.23	0.0
Acute nonlymphocytic	0	0.10	0.0	0	0.07	0.0	0	0.01	0.0	0	0.02	0.0	0	0.20	0.0

[a] ICD-O code = 150.

[b] $P < .05$.

ESOPHAGUS
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the esophagus among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	706			212			35			10			706		
Person-yr in interval	320			287			94			64			765		
Second primary cancer site	O	F	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**6**	**3.25**	**1.8**	**5**	**3.14**	**1.6**	**1**	**1.10**	**0.9**	**0**	**0.89**	**0.0**	**12**	**8.38**	**1.4**
All excluding site of initial cancer	**6**	**3.22**	**1.9**	**4**	**3.12**	**1.3**	**1**	**1.09**	**0.9**	**0**	**0.88**	**0.0**	**11**	**8.31**	**1.3**
Buccal cavity, pharynx	**2**	**0.06**	**34.2**[b]	**2**	**0.06**	**35.5**[b]	**1**	**0.02**	**53.5**	**0**	**0.02**	**0.0**	**5**	**0.15**	**33.5**[b]
Lip	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Tongue	1	0.01	85.7[b]	2	0.01	169.5[b]	0	0.00	0.0	0	0.00	0.0	3	0.03	97.8[b]
Salivary gland	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Gum, other mouth	1	0.02	48.1	0	0.02	0.0	1	0.01	160.9[b]	0	0.01	0.0	2	0.05	38.0[b]
Pharynx	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Digestive system	**1**	**1.03**	**1.0**	**2**	**1.02**	**2.0**	**0**	**0.39**	**0.0**	**0**	**0.31**	**0.0**	**3**	**2.74**	**1.1**
Esophagus	0	0.03	0.0	1	0.02	41.1	0	0.01	0.0	0	0.01	0.0	1	0.07	15.3
Stomach	0	0.14	0.0	0	0.14	0.0	0	0.06	0.0	0	0.04	0.0	0	0.38	0.0
Colon	0	0.48	0.0	1	0.47	2.1	0	0.18	0.0	0	0.15	0.0	1	1.28	0.8
Rectum	1	0.19	5.2	0	0.19	0.0	0	0.07	0.0	0	0.06	0.0	1	0.50	2.0
Liver, biliary	0	0.07	0.0	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.19	0.0
Pancreas	0	0.10	0.0	0	0.10	0.0	0	0.04	0.0	0	0.03	0.0	0	0.28	0.0
Respiratory system	**1**	**0.22**	**4.6**	**0**	**0.21**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.06**	**0.0**	**1**	**0.55**	**1.8**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Larynx	1	0.01	81.6[b]	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	1	0.03	32.9
Trachea, bronchus, lung	0	0.20	0.0	0	0.19	0.0	0	0.05	0.0	0	0.05	0.0	0	0.49	0.0
Female breast	1	0.83	1.2	0	0.78	0.0	0	0.26	0.0	0	0.21	0.0	1	2.08	0.5
Female genital tract	**0**	**0.50**	**0.0**	**1**	**0.47**	**2.1**	**0**	**0.15**	**0.0**	**0**	**0.11**	**0.0**	**1**	**1.23**	**0.8**
Cervix uteri	0	0.09	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.21	0.0
Corpus uteri	0	0.21	0.0	0	0.19	0.0	0	0.06	0.0	0	0.05	0.0	0	0.51	0.0
Uterus, NOS	0	0.04	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Ovary, fallopian tubes	0	0.13	0.0	1	0.13	7.9	0	0.04	0.0	0	0.03	0.0	1	0.33	3.0
Kidney, renal pelvis, ureter	0	0.05	0.0	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.13	0.0
Bladder, other urinary	0	0.09	0.0	0	0.09	0.0	0	0.04	0.0	0	0.03	0.0	0	0.26	0.0
Melanoma of the skin	0	0.04	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Eye	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Brain, central nervous system	0	0.03	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Thyroid gland	1	0.02	46.9	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	1	0.05	18.9
Bone	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Connective tissue	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Lymphatic, hematopoietic system	**0**	**0.21**	**0.0**	**0**	**0.20**	**0.0**	**0**	**0.07**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.54**	**0.0**
Non-Hodgkin's lymphoma	0	0.08	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.21	0.0
Hodgkin's disease	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Multiple myeloma	0	0.04	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Leukemias	0	0.08	0.0	0	0.07	0.0	0	0.03	0.0	0	0.03	0.0	0	0.21	0.0
Chronic lymphocytic	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0

[a] ICD-O code = 150.

[b] $P < .05$.

STOMACH
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the stomach, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	6,478	3,770	10,248
No. who developed a second primary cancer	175	76	251
Average age at diagnosis of first cancer, yr	64	66	65
Average yr of diagnosis of first cancer	1961	1961	1961
Person-yr of follow-up	11,251	7,520	18,771
Average follow-up, yr	1.7	2.0	1.8
Percent given radiotherapy for first cancer	6.8	4.7	6.0

[a] ICD-O code = 151.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the stomach in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	211	84.1
Only the first cancer	26	10.4
Only the second cancer	11	4.4
Neither first nor second cancer	3	1.2
Total second primary cancers	251	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

STOMACH
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the stomach among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	10,248			3,958			969			495			10,248		
Person-yr in interval	4,903			7,032			3,387			3,448			18,771		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**54**	**59.84**	**0.9**	**86**	**87.75**	**1.0**	**43**	**48.85**	**0.9**	**68**	**61.46**	**1.1**	**251**	**257.71**	**1.0**
All excluding site of initial cancer	**54**	**56.05**	**1.0**	**84**	**82.48**	**1.0**	**43**	**45.99**	**0.9**	**68**	**58.12**	**1.2**	**249**	**242.46**	**1.0**
Buccal cavity, pharynx	**2**	**2.50**	**0.8**	**3**	**3.54**	**0.8**	**1**	**1.86**	**0.5**	**1**	**2.12**	**0.5**	**7**	**10.01**	**0.7**
Lip	1	0.48	2.1	0	0.66	0.0	0	0.36	0.0	1	0.39	2.5	2	1.88	1.1
Tongue	0	0.50	0.0	1	0.70	1.4	0	0.36	0.0	0	0.41	0.0	1	1.97	0.5
Salivary gland	0	0.15	0.0	0	0.22	0.0	0	0.12	0.0	0	0.15	0.0	0	0.64	0.0
Gum, other mouth	0	0.70	0.0	1	1.00	1.0	0	0.52	0.0	0	0.60	0.0	1	2.82	0.4
Pharynx	1	0.58	1.7	1	0.84	1.2	1	0.43	2.3	0	0.48	0.0	3	2.33	1.3
Digestive system	**13**	**20.21**	**0.6**	**26**	**29.42**	**0.9**	**13**	**16.46**	**0.8**	**15**	**20.63**	**0.7**	**67**	**86.66**	**0.8**[b]
Esophagus	1	1.08	0.9	1	1.54	0.6	2	0.82	2.4	1	0.92	1.1	5	4.36	1.1
Stomach	0	3.79	0.0[b]	2	5.27	0.4	0	2.86	0.0	0	3.34	0.0	2	15.25	0.1[b]
Colon	5	7.83	0.6	12	11.65	1.0	6	6.67	0.9	9	8.79	1.0	32	34.91	0.9
Rectum	0	3.99	0.0[b]	5	5.82	0.9	1	3.22	0.3	4	3.93	1.0	10	16.94	0.6
Liver, biliary	2	1.16	1.7	2	1.69	1.2	2	0.94	2.1	1	1.20	0.8	7	4.99	1.4
Pancreas	3	1.99	1.5	4	2.93	1.4	2	1.66	1.2	0	2.11	0.0	9	8.68	1.0
Respiratory system	**3**	**8.74**	**0.3**	**15**	**12.84**	**1.2**	**5**	**6.95**	**0.7**	**15**	**8.44**	**1.8**	**38**	**36.93**	**1.0**
Nasal cavities, sinuses	0	0.12	0.0	0	0.18	0.0	1	0.10	10.2	0	0.12	0.0	1	0.52	1.9
Larynx	0	0.97	0.0	2	1.40	1.4	0	0.72	0.0	1	0.79	1.3	3	3.87	0.8
Trachea, bronchus, lung	3	7.56	0.4	13	11.14	1.2	4	6.07	0.7	14	7.46	1.9[b]	34	32.21	1.1
Female breast	6	4.46	1.3	8	7.14	1.1	2	3.82	0.5	9	4.58	2.0	25	19.99	1.3
Female genital tract	**3**	**2.90**	**1.0**	**0**	**4.48**	**0.0**[b]	**3**	**2.30**	**1.3**	**2**	**2.46**	**0.8**	**8**	**12.12**	**0.7**
Cervix uteri	0	0.59	0.0	0	0.85	0.0	0	0.41	0.0	0	0.38	0.0	0	2.22	0.0
Corpus uteri	0	1.05	0.0	0	1.72	0.0	1	0.90	1.1	1	1.00	1.0	2	4.67	0.4
Uterus, NOS	0	0.29	0.0	0	0.39	0.0	1	0.19	5.3	0	0.17	0.0	1	1.05	1.0
Ovary, fallopian tubes	2	0.77	2.6	0	1.21	0.0	1	0.63	1.6	1	0.69	1.5	4	3.30	1.2
Prostate gland	13	7.52	1.7	10	10.48	1.0	3	6.40	0.5	12	9.10	1.3	38	33.47	1.1
Testis	0	0.06	0.0	1	0.09	11.4	0	0.04	0.0	0	0.04	0.0	1	0.23	4.4
Kidney, renal pelvis, ureter	6	1.28	4.7[b]	5	1.88	2.7	0	1.03	0.0	1	1.24	0.8	12	5.43	2.2[b]
Bladder, other urinary	4	3.46	1.2	7	5.00	1.4	8	2.86	2.8[b]	4	3.84	1.0	23	15.15	1.5
Melanoma of the skin	0	0.56	0.0	0	0.83	0.0	0	0.43	0.0	1	0.54	1.9	1	2.36	0.4
Eye	1	0.09	10.7	0	0.14	0.0	0	0.07	0.0	0	0.08	0.0	1	0.39	2.6
Brain, central nervous system	0	0.54	0.0	1	0.82	1.2	0	0.41	0.0	0	0.42	0.0	1	2.18	0.5
Thyroid gland	0	0.23	0.0	0	0.34	0.0	0	0.18	0.0	0	0.20	0.0	0	0.95	0.0
Bone	0	0.10	0.0	0	0.13	0.0	0	0.07	0.0	0	0.07	0.0	0	0.36	0.0
Connective tissue	0	0.28	0.0	2	0.41	4.9	1	0.23	4.4	0	0.29	0.0	3	1.21	2.5
Lymphatic, hematopoietic system	**2**	**3.85**	**0.5**	**6**	**5.72**	**1.0**	**5**	**3.21**	**1.6**	**6**	**4.20**	**1.4**	**19**	**16.97**	**1.1**
Non-Hodgkin's lymphoma	0	1.26	0.0	2	1.90	1.1	1	1.03	1.0	1	1.31	0.8	4	5.50	0.7
Hodgkin's disease	0	0.27	0.0	0	0.39	0.0	0	0.20	0.0	1	0.22	4.6	1	1.09	0.9
Multiple myeloma	0	0.59	0.0	0	0.90	0.0	2	0.52	3.9	1	0.70	1.4	3	2.70	1.1
Leukemias	2	1.72	1.2	4	2.53	1.6	2	1.45	1.4	3	1.98	1.5	11	7.67	1.4
Chronic lymphocytic	0	0.53	0.0	2	0.77	2.6	1	0.45	2.2	0	0.65	0.0	3	2.40	1.3
Acute nonlymphocytic	2	0.48	4.1	1	0.73	1.4	0	0.42	0.0	3	0.61	5.0	6	2.23	2.7

[a] ICD-O code = 151.
[b] $P < .05$.

STOMACH
MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the stomach among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,478			2,447			579			285			6,478		
Person-yr in interval	3,070			4,224			1,982			1,975			11,251		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**39**	**41.36**	**0.9**	**61**	**58.11**	**1.0**	**33**	**32.71**	**1.0**	**42**	**41.60**	**1.0**	**175**	**173.66**	**1.0**
All excluding site of initial cancer	**39**	**38.53**	**1.0**	**59**	**54.28**	**1.1**	**33**	**30.64**	**1.1**	**42**	**39.19**	**1.1**	**173**	**162.52**	**1.1**
Buccal cavity, pharynx	**2**	**2.20**	**0.9**	**3**	**3.06**	**1.0**	**1**	**1.60**	**0.6**	**1**	**1.80**	**0.6**	**7**	**8.65**	**0.8**
Lip	1	0.45	2.2	0	0.62	0.0	0	0.34	0.0	1	0.37	2.7	2	1.78	1.1
Tongue	0	0.44	0.0	1	0.61	1.7	0	0.31	0.0	0	0.34	0.0	1	1.70	0.6
Salivary gland	0	0.11	0.0	0	0.15	0.0	0	0.08	0.0	0	0.11	0.0	0	0.45	0.0
Gum, other mouth	0	0.60	0.0	1	0.83	1.2	0	0.43	0.0	0	0.48	0.0	1	2.33	0.4
Pharynx	1	0.52	1.9	1	0.74	1.4	1	0.38	2.6	0	0.43	0.0	3	2.06	1.5
Digestive system	**8**	**13.86**	**0.6**	**18**	**19.30**	**0.9**	**12**	**10.79**	**1.1**	**8**	**13.38**	**0.6**	**46**	**57.29**	**0.8**
Esophagus	0	0.95	0.0	1	1.33	0.8	2	0.71	2.8	1	0.77	1.3	4	3.76	1.1
Stomach	0	2.83	0.0	2	3.83	0.5	0	2.07	0.0	0	2.41	0.0	2	11.14	0.2[b]
Colon	2	4.93	0.4	7	6.93	1.0	6	4.00	1.5	4	5.28	0.8	19	21.12	0.9
Rectum	0	2.84	0.0	4	3.98	1.0	0	2.20	0.0	3	2.65	1.1	7	11.66	0.6
Liver, biliary	1	0.70	1.4	2	0.96	2.1	2	0.54	3.7	0	0.70	0.0	5	2.90	1.7
Pancreas	3	1.37	2.2	2	1.93	1.0	2	1.09	1.8	0	1.36	0.0	7	5.75	1.2
Respiratory system	**3**	**7.82**	**0.4**	**14**	**11.24**	**1.2**	**5**	**6.11**	**0.8**	**13**	**7.38**	**1.8**	**35**	**32.53**	**1.1**
Nasal cavities, sinuses	0	0.09	0.0	0	0.13	0.0	1	0.07	14.2	0	0.09	0.0	1	0.38	2.6
Larynx	0	0.92	0.0	2	1.31	1.5	0	0.68	0.0	1	0.74	1.4	3	3.64	0.8
Trachea, bronchus, lung	3	6.74	0.4	12	9.70	1.2	4	5.31	0.8	12	6.49	1.8	31	28.23	1.1
Prostate gland	13	7.52	1.7	10	10.48	1.0	3	6.40	0.5	12	9.10	1.3	38	33.47	1.1
Testis	0	0.06	0.0	1	0.09	11.4	0	0.04	0.0	0	0.04	0.0	1	0.23	4.4
Kidney, renal pelvis, ureter	6	0.99	6.0[b]	5	1.41	3.5[b]	0	0.77	0.0	0	0.93	0.0	11	4.11	2.7[b]
Bladder, other urinary	4	2.91	1.4	6	4.10	1.5	8	2.34	3.4[b]	3	3.14	1.0	21	12.48	1.7[b]
Melanoma of the skin	0	0.39	0.0	0	0.54	0.0	0	0.28	0.0	1	0.35	2.9	1	1.56	0.6
Eye	1	0.06	16.3	0	0.09	0.0	0	0.05	0.0	0	0.05	0.0	1	0.24	4.1
Brain, central nervous system	0	0.39	0.0	0	0.57	0.0	0	0.28	0.0	0	0.28	0.0	0	1.52	0.0
Thyroid gland	0	0.10	0.0	0	0.15	0.0	0	0.08	0.0	0	0.08	0.0	0	0.41	0.0
Bone	0	0.07	0.0	0	0.09	0.0	0	0.04	0.0	0	0.04	0.0	0	0.24	0.0
Connective tissue	0	0.20	0.0	2	0.29	7.0	1	0.16	6.3	0	0.20	0.0	3	0.85	3.5
Lymphatic, hematopoietic system	**1**	**2.67**	**0.4**	**2**	**3.76**	**0.5**	**1**	**2.11**	**0.5**	**2**	**2.75**	**0.7**	**6**	**11.28**	**0.5**
Non-Hodgkin's lymphoma	0	0.84	0.0	0	1.19	0.0	0	0.65	0.0	0	0.81	0.0	0	3.49	0.0
Hodgkin's disease	0	0.19	0.0	0	0.27	0.0	0	0.14	0.0	1	0.15	6.8	1	0.75	1.3
Multiple myeloma	0	0.39	0.0	0	0.56	0.0	0	0.32	0.0	0	0.43	0.0	0	1.70	0.0
Leukemias	1	1.24	0.8	2	1.75	1.1	1	1.01	1.0	1	1.36	0.7	5	5.35	0.9
Chronic lymphocytic	0	0.39	0.0	2	0.55	3.6	0	0.32	0.0	0	0.46	0.0	2	1.73	1.2
Acute nonlymphocytic	1	0.34	3.0	0	0.48	0.0	0	0.28	0.0	1	0.40	2.5	2	1.50	1.3

[a] ICD-O code = 151.

[b] $P < .05$.

STOMACH
FEMALES

TABLE 2E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the stomach among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,770			1,511			390			210			3,770		
Person-yr in interval	1,834			2,808			1,405			1,473			7,520		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**15**	**18.47**	**0.8**	**25**	**29.64**	**0.8**	**10**	**16.14**	**0.6**	**26**	**19.86**	**1.3**	**76**	**84.05**	**0.9**
All excluding site of initial cancer	**15**	**17.51**	**0.9**	**25**	**28.21**	**0.9**	**10**	**15.35**	**0.7**	**26**	**18.93**	**1.4**	**76**	**79.94**	**1.0**
Buccal cavity, pharynx	**0**	**0.30**	**0.0**	**0**	**0.49**	**0.0**	**0**	**0.26**	**0.0**	**0**	**0.32**	**0.0**	**0**	**1.36**	**0.0**
Lip	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Tongue	0	0.06	0.0	0	0.10	0.0	0	0.05	0.0	0	0.06	0.0	0	0.27	0.0
Salivary gland	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.05	0.0	0	0.19	0.0
Gum, other mouth	0	0.10	0.0	0	0.17	0.0	0	0.09	0.0	0	0.12	0.0	0	0.49	0.0
Pharynx	0	0.06	0.0	0	0.10	0.0	0	0.05	0.0	0	0.06	0.0	0	0.27	0.0
Digestive system	**5**	**6.35**	**0.8**	**8**	**10.13**	**0.8**	**1**	**5.67**	**0.2**[b]	**7**	**7.25**	**1.0**	**21**	**29.37**	**0.7**
Esophagus	1	0.13	7.6	0	0.21	0.0	0	0.12	0.0	0	0.15	0.0	1	0.60	1.7
Stomach	0	0.96	0.0	0	1.43	0.0	0	0.79	0.0	0	0.93	0.0	0	4.11	0.0[b]
Colon	3	2.90	1.0	5	4.72	1.1	0	2.67	0.0	5	3.51	1.4	13	13.79	0.9
Rectum	0	1.15	0.0	1	1.84	0.5	1	1.01	1.0	1	1.28	0.8	3	5.28	0.6
Liver, biliary	1	0.46	2.2	0	0.72	0.0	0	0.40	0.0	1	0.50	2.0	2	2.09	1.0
Pancreas	0	0.62	0.0	2	1.00	2.0	0	0.57	0.0	0	0.75	0.0	2	2.93	0.7
Respiratory system	**0**	**0.92**	**0.0**	**1**	**1.59**	**0.6**	**0**	**0.84**	**0.0**	**2**	**1.06**	**1.9**	**3**	**4.41**	**0.7**
Nasal cavities, sinuses	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.14	0.0
Larynx	0	0.05	0.0	0	0.09	0.0	0	0.04	0.0	0	0.05	0.0	0	0.23	0.0
Trachea, bronchus, lung	0	0.83	0.0	1	1.44	0.7	0	0.76	0.0	2	0.97	2.1	3	3.98	0.8
Female breast	6	4.46	1.3	8	7.14	1.1	2	3.82	0.5	9	4.58	2.0	25	19.99	1.3
Female genital tract	**3**	**2.90**	**1.0**	**0**	**4.48**	**0.0**[b]	**3**	**2.30**	**1.3**	**2**	**2.46**	**0.8**	**8**	**12.12**	**0.7**
Cervix uteri	0	0.59	0.0	0	0.85	0.0	0	0.41	0.0	0	0.38	0.0	0	2.22	0.0
Corpus uteri	0	1.05	0.0	0	1.72	0.0	1	0.90	1.1	1	1.00	1.0	2	4.67	0.4
Uterus, NOS	0	0.29	0.0	0	0.39	0.0	1	0.19	5.3	0	0.17	0.0	1	1.05	1.0
Ovary, fallopian tubes	2	0.77	2.6	0	1.21	0.0	1	0.63	1.6	1	0.69	1.5	4	3.30	1.2
Kidney, renal pelvis, ureter	0	0.29	0.0	0	0.47	0.0	0	0.26	0.0	1	0.31	3.2	1	1.32	0.8
Bladder, other urinary	0	0.55	0.0	1	0.90	1.1	0	0.52	0.0	1	0.70	1.4	2	2.67	0.7
Melanoma of the skin	0	0.17	0.0	0	0.29	0.0	0	0.15	0.0	0	0.19	0.0	0	0.80	0.0
Eye	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.15	0.0
Brain, central nervous system	0	0.15	0.0	1	0.25	4.0	0	0.13	0.0	0	0.13	0.0	1	0.66	1.5
Thyroid gland	0	0.12	0.0	0	0.19	0.0	0	0.10	0.0	0	0.12	0.0	0	0.54	0.0
Bone	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.12	0.0
Connective tissue	0	0.08	0.0	0	0.13	0.0	0	0.07	0.0	0	0.08	0.0	0	0.35	0.0
Lymphatic, hematopoietic system	**1**	**1.18**	**0.8**	**4**	**1.96**	**2.0**	**4**	**1.09**	**3.7**	**4**	**1.46**	**2.7**	**13**	**5.68**	**2.3**[b]
Non-Hodgkin's lymphoma	0	0.42	0.0	2	0.71	2.8	1	0.39	2.6	1	0.50	2.0	4	2.02	2.0
Hodgkin's disease	0	0.08	0.0	0	0.12	0.0	0	0.07	0.0	0	0.07	0.0	0	0.34	0.0
Multiple myeloma	0	0.20	0.0	0	0.34	0.0	2	0.19	10.5[b]	1	0.27	3.7	3	0.99	3.0
Leukemias	1	0.48	2.1	2	0.78	2.6	1	0.44	2.3	2	0.61	3.3	6	2.31	2.6
Chronic lymphocytic	0	0.13	0.0	0	0.22	0.0	1	0.13	7.7	0	0.19	0.0	1	0.67	1.5
Acute nonlymphocytic	1	0.15	6.9	1	0.24	4.1	0	0.14	0.0	2	0.20	9.9[b]	4	0.73	5.5[b]

[a] ICD-O code = 151.

[b] $P < .05$.

SMALL INTESTINE
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the small intestine, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	271	283	554
No. who developed a second primary cancer	26	15	41
Average age at diagnosis of first cancer, yr	61	60	60
Average yr of diagnosis of first cancer	1966	1966	1966
Person-yr of follow-up	1,002	1,102	2,104
Average follow-up, yr	3.7	3.9	3.8
Percent given radiotherapy for first cancer	5.9	2.8	4.3

[a] ICD-O code = 152.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the small intestine in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	39	95.1
Only the first cancer	2	4.9
Only the second cancer	0	0.0
Neither first nor second cancer	0	0.0
Total second primary cancers	41	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

SMALL INTESTINE
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the small intestine among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	554			354			132			67			554		
Person-yr in interval	361			812			477			453			2,104		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8**	**3.67**	**2.2**	**18**	**8.56**	**2.1**[b]	**7**	**5.45**	**1.3**	**8**	**5.95**	**1.3**	**41**	**23.61**	**1.7**[b]
All excluding site of initial cancer	**8**	**3.66**	**2.2**	**17**	**8.54**	**2.0**[b]	**7**	**5.44**	**1.3**	**8**	**5.93**	**1.3**	**40**	**23.55**	**1.7**[b]
Buccal cavity, pharynx	**0**	**0.14**	**0.0**	**0**	**0.32**	**0.0**	**0**	**0.19**	**0.0**	**0**	**0.20**	**0.0**	**0**	**0.85**	**0.0**
Lip	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.12	0.0
Tongue	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.17	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Gum, other mouth	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.25	0.0
Pharynx	0	0.03	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.21	0.0
Digestive system	**3**	**1.13**	**2.7**	**6**	**2.62**	**2.3**	**3**	**1.67**	**1.8**	**5**	**1.84**	**2.7**	**17**	**7.25**	**2.3**[b]
Esophagus	0	0.06	0.0	0	0.13	0.0	0	0.08	0.0	0	0.09	0.0	0	0.36	0.0
Stomach	0	0.18	0.0	1	0.39	2.5	0	0.24	0.0	1	0.25	3.9	2	1.06	1.9
Colon	0	0.46	0.0	2	1.09	1.8	2	0.72	2.8	3	0.80	3.7	7	3.07	2.3
Rectum	0	0.23	0.0	0	0.54	0.0	1	0.33	3.0	1	0.36	2.7	2	1.46	1.4
Liver, biliary	2	0.07	30.7[b]	0	0.15	0.0	0	0.10	0.0	0	0.11	0.0	2	0.42	4.8
Pancreas	1	0.11	8.7	2	0.27	7.4	0	0.18	0.0	0	0.20	0.0	3	0.76	4.0
Respiratory system	**1**	**0.56**	**1.8**	**2**	**1.35**	**1.5**	**0**	**0.81**	**0.0**	**0**	**0.87**	**0.0**	**3**	**3.59**	**0.8**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.06	0.0	0	0.14	0.0	0	0.08	0.0	0	0.08	0.0	0	0.36	0.0
Trachea, bronchus, lung	1	0.49	2.1	2	1.18	1.7	0	0.72	0.0	0	0.77	0.0	3	3.15	1.0
Female breast	1	0.41	2.4	1	0.94	1.1	1	0.63	1.6	0	0.71	0.0	3	2.68	1.1
Female genital tract	**1**	**0.26**	**3.9**	**2**	**0.59**	**3.4**	**0**	**0.39**	**0.0**	**0**	**0.39**	**0.0**	**3**	**1.63**	**1.8**
Cervix uteri	0	0.05	0.0	1	0.11	9.2	0	0.07	0.0	0	0.06	0.0	1	0.28	3.5
Corpus uteri	0	0.11	0.0	0	0.25	0.0	0	0.17	0.0	0	0.19	0.0	0	0.72	0.0
Uterus, NOS	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.09	0.0
Ovary, fallopian tubes	1	0.07	14.4	1	0.16	6.2	0	0.11	0.0	0	0.11	0.0	2	0.45	4.4
Prostate gland	1	0.35	2.8	3	0.82	3.6	1	0.53	1.9	2	0.59	3.4	7	2.29	3.1[b]
Testis	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.02	0.0
Kidney, renal pelvis, ureter	0	0.08	0.0	1	0.19	5.2	0	0.12	0.0	0	0.12	0.0	1	0.51	2.0
Bladder, other urinary	1	0.19	5.1	0	0.46	0.0	0	0.29	0.0	0	0.33	0.0	1	1.27	0.8
Melanoma of the skin	0	0.04	0.0	1	0.10	10.1	0	0.06	0.0	0	0.07	0.0	1	0.27	3.7
Eye	0	0.01	0.0	1	0.01	74.1	0	0.01	0.0	0	0.01	0.0	1	0.04	28.0
Brain, central nervous system	0	0.04	0.0	1	0.10	10.2	0	0.06	0.0	0	0.06	0.0	1	0.26	3.9
Thyroid gland	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Connective tissue	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**0**	**0.24**	**0.0**	**0**	**0.57**	**0.0**	**2**	**0.37**	**5.5**	**1**	**0.41**	**2.4**	**3**	**1.59**	**1.9**
Non-Hodgkin's lymphoma	0	0.09	0.0	0	0.20	0.0	0	0.13	0.0	1	0.14	7.0	1	0.56	1.8
Hodgkin's disease	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Multiple myeloma	0	0.04	0.0	0	0.09	0.0	1	0.06	15.9	0	0.07	0.0	1	0.27	3.7
Leukemias	0	0.10	0.0	0	0.23	0.0	1	0.15	6.7	0	0.17	0.0	1	0.65	1.5
Chronic lymphocytic	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.06	0.0	0	0.21	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.07	0.0	1	0.05	20.9	0	0.06	0.0	1	0.21	4.8

[a] ICD-O code = 152.

[b] $P < .05$.

COLON
BOTH SEXES

TABLE 4A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the colon, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	12,324	14,480	26,804
No. who developed a second primary cancer	1,190	1,078	2,268
Average age at diagnosis of first cancer, yr	66	66	66
Average yr of diagnosis of first cancer	1966	1965	1966
Person-yr of follow-up	50,832	70,476	121,309
Average follow-up, yr	4.1	4.9	4.5
Percent given radiotherapy for first cancer	2.4	2.3	2.3

[a] ICD-O codes = 153, 159.0.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the colon in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	2,028	89.4
Only the first cancer	190	8.4
Only the second cancer	39	1.7
Neither first nor second cancer	11	0.5
Total second primary cancers	2,268	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

COLON
BOTH SEXES

TABLE 4C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the colon among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	26,804			18,813			8,071			3,984			26,804		
Person-yr in interval	18,167			47,697			28,621			26,825			121,309		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**284**	**234.47**	**1.2**[b]	**860**	**642.43**	**1.3**[b]	**515**	**412.53**	**1.2**[b]	**609**	**426.06**	**1.4**[b]	**2,268**	**1,714.37**	**1.3**[b]
All excluding site of initial cancer	**236**	**202.16**	**1.2**[b]	**676**	**552.97**	**1.2**[b]	**395**	**353.20**	**1.1**[b]	**455**	**361.58**	**1.3**[b]	**1,762**	**1,468.95**	**1.2**[b]
Buccal cavity, pharynx	**13**	**7.99**	**1.6**	**22**	**21.25**	**1.0**	**15**	**12.89**	**1.2**	**16**	**11.93**	**1.3**	**66**	**54.02**	**1.2**
Lip	0	1.30	0.0	6	3.39	1.8	2	2.05	1.0	2	1.82	1.1	10	8.55	1.2
Tongue	2	1.59	1.3	4	4.19	1.0	7	2.53	2.8[b]	4	2.32	1.7	17	10.62	1.6
Salivary gland	1	0.56	1.8	4	1.52	2.6	0	0.98	0.0	1	1.00	1.0	6	4.06	1.5
Gum, other mouth	4	2.35	1.7	1	6.28	0.2[b]	3	3.84	0.8	5	3.65	1.4	13	16.11	0.8
Pharynx	4	1.90	2.1	6	5.06	1.2	3	3.02	1.0	3	2.70	1.1	16	12.67	1.3
Digestive system	**96**	**76.46**	**1.3**[b]	**379**	**208.96**	**1.8**[b]	**208**	**135.70**	**1.5**[b]	**262**	**141.70**	**1.8**[b]	**945**	**562.46**	**1.7**[b]
Esophagus	5	3.44	1.5	10	9.13	1.1	5	5.54	0.9	5	5.16	1.0	25	23.24	1.1
Stomach	6	12.15	0.5	41	32.35	1.3	20	20.39	1.0	21	19.78	1.1	88	84.61	1.0
Colon	48	32.31	1.5[b]	184	89.46	2.1[b]	120	59.33	2.0[b]	154	64.48	2.4[b]	506	245.42	2.1[b]
Rectum	20	15.00	1.3	95	40.85	2.3[b]	41	26.17	1.6[b]	48	26.75	1.8[b]	204	108.70	1.9[b]
Liver, biliary	5	4.50	1.1	8	12.33	0.6	9	8.11	1.1	15	8.52	1.8	37	33.45	1.1
Pancreas	8	7.71	1.0	24	21.20	1.1	9	13.84	0.7	16	14.67	1.1	57	57.38	1.0
Respiratory system	**12**	**31.68**	**0.4**[b]	**80**	**86.42**	**0.9**	**63**	**52.81**	**1.2**	**44**	**51.01**	**0.9**	**199**	**221.76**	**0.9**
Nasal cavities, sinuses	1	0.45	2.2	1	1.21	0.8	2	0.76	2.6	0	0.74	0.0	4	3.15	1.3
Larynx	1	3.10	0.3	6	8.25	0.7	8	4.83	1.7	4	4.25	0.9	19	20.41	0.9
Trachea, bronchus, lung	9	27.83	0.3[b]	72	76.15	0.9	53	46.73	1.1	38	45.54	0.8	172	196.12	0.9
Female breast	22	25.16	0.9	79	69.24	1.1	50	46.59	1.1	81	52.36	1.5[b]	232	193.23	1.2[b]
Female genital tract	**43**	**15.57**	**2.8**[b]	**83**	**42.10**	**2.0**[b]	**28**	**27.40**	**1.0**	**46**	**28.75**	**1.6**[b]	**200**	**113.76**	**1.8**[b]
Cervix uteri	9	2.89	3.1[b]	8	7.52	1.1	4	4.63	0.9	2	4.36	0.5	23	19.38	1.2
Corpus uteri	8	6.22	1.3	31	17.14	1.8[b]	13	11.32	1.1	28	12.33	2.3[b]	80	46.97	1.7[b]
Uterus, NOS	3	1.18	2.6	1	2.99	0.3	1	1.85	0.5	6	1.60	3.8[b]	11	7.61	1.4
Ovary, fallopian tubes	22	4.26	5.2[b]	39	11.61	3.4[b]	7	7.61	0.9	9	8.14	1.1	77	31.60	2.4[b]
Prostate gland	41	25.57	1.6[b]	83	71.33	1.2	61	45.03	1.4[b]	59	44.37	1.3[b]	244	186.18	1.3[b]
Testis	0	0.17	0.0	0	0.42	0.0	0	0.23	0.0	0	0.18	0.0	0	0.99	0.0
Kidney, renal pelvis, ureter	8	4.80	1.7	15	13.07	1.1	10	8.22	1.2	15	8.19	1.8[b]	48	34.25	1.4[b]
Bladder, other urinary	19	12.74	1.5	37	35.23	1.1	21	22.57	0.9	24	23.30	1.0	101	93.78	1.1
Melanoma of the skin	7	2.34	3.0[b]	7	6.41	1.1	8	4.01	2.0	2	4.13	0.5	24	16.87	1.4
Eye	0	0.35	0.0	0	0.95	0.0	3	0.59	5.0[b]	1	0.59	1.7	4	2.48	1.6
Brain, central nervous system	1	2.13	0.5	10	5.72	1.7	7	3.45	2.0	5	3.29	1.5	23	14.58	1.6
Thyroid gland	3	0.97	3.1	2	2.63	0.8	2	1.68	1.2	2	1.72	1.2	9	7.00	1.3
Bone	0	0.33	0.0	3	0.84	3.6	0	0.51	0.0	0	0.46	0.0	3	2.14	1.4
Connective tissue	3	1.06	2.8	2	2.88	0.7	3	1.84	1.6	3	1.88	1.6	11	7.66	1.4
Lymphatic, hematopoietic system	**14**	**15.48**	**0.9**	**46**	**42.89**	**1.1**	**26**	**28.03**	**0.9**	**36**	**30.11**	**1.2**	**122**	**116.43**	**1.0**
Non-Hodgkin's lymphoma	7	5.23	1.3	15	14.47	1.0	6	9.37	0.6	14	9.99	1.4	42	39.04	1.1
Hodgkin's disease	1	0.99	1.0	2	2.64	0.8	2	1.61	1.2	3	1.54	1.9	8	6.78	1.2
Multiple myeloma	1	2.55	0.4	10	7.16	1.4	5	4.78	1.0	5	5.33	0.9	21	19.81	1.1
Leukemias	5	6.69	0.7	19	18.59	1.0	13	12.26	1.1	14	13.24	1.1	51	50.74	1.0
Chronic lymphocytic	1	2.09	0.5	5	5.86	0.9	3	3.91	0.8	4	4.29	0.9	13	16.14	0.8
Acute nonlymphocytic	2	2.06	1.0	6	5.81	1.0	4	3.87	1.0	8	4.37	1.8	20	16.10	1.2

[a] ICD-O codes = 153, 159.0.

[b] $P < .05$.

COLON
MALES

TABLE 4D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the colon among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	12,324			8,531			3,444			1,583			12,324		
Person-yr in interval	8,275			21,190			11,781			9,586			50,832		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**143**	**131.76**	**1.1**	**471**	**358.36**	**1.3^b**	**283**	**218.01**	**1.3^b**	**293**	**203.19**	**1.4^b**	**1,190**	**910.70**	**1.3^b**
All excluding site of initial cancer	**119**	**115.66**	**1.0**	**373**	**314.25**	**1.2^b**	**228**	**190.83**	**1.2^b**	**226**	**177.23**	**1.3^b**	**946**	**797.41**	**1.2^b**
Buccal cavity, pharynx	**10**	**6.28**	**1.6**	**18**	**16.52**	**1.1**	**10**	**9.69**	**1.0**	**9**	**8.32**	**1.1**	**47**	**40.78**	**1.2**
Lip	0	1.18	0.0	6	3.07	2.0	2	1.82	1.1	1	1.55	0.6	9	7.61	1.2
Tongue	2	1.24	1.6	4	3.22	1.2	4	1.87	2.1	2	1.59	1.3	12	7.92	1.5
Salivary gland	1	0.33	3.0	1	0.90	1.1	0	0.56	0.0	1	0.52	1.9	3	2.32	1.3
Gum, other mouth	2	1.74	1.1	1	4.59	0.2	1	2.68	0.4	3	2.31	1.3	7	11.32	0.6
Pharynx	3	1.54	1.9	5	4.08	1.2	3	2.38	1.3	2	2.03	1.0	13	10.02	1.3
Digestive system	**50**	**42.35**	**1.2**	**220**	**114.11**	**1.9^b**	**106**	**69.10**	**1.5^b**	**122**	**63.57**	**1.9^b**	**498**	**288.94**	**1.7^b**
Esophagus	3	2.71	1.1	6	7.13	0.8	3	4.16	0.7	3	3.55	0.8	15	17.54	0.9
Stomach	5	7.67	0.7	32	20.19	1.6^b	11	12.02	0.9	13	10.62	1.2	61	50.46	1.2
Colon	24	16.10	1.5	98	44.11	2.2^b	55	27.18	2.0^b	67	25.96	2.6^b	244	113.29	2.2^b
Rectum	13	8.71	1.5	59	23.36	2.5^b	23	14.01	1.6^b	20	12.64	1.6	115	58.68	2.0^b
Liver, biliary	2	2.16	0.9	5	5.87	0.9	6	3.59	1.7	7	3.34	2.1	20	14.95	1.3
Pancreas	2	4.29	0.5	13	11.59	1.1	6	7.03	0.9	11	6.47	1.7	32	29.35	1.1
Respiratory system	**8**	**25.75**	**0.3^b**	**63**	**69.81**	**0.9**	**49**	**41.60**	**1.2**	**37**	**37.78**	**1.0**	**157**	**174.83**	**0.9**
Nasal cavities, sinuses	1	0.28	3.6	0	0.75	0.0	0	0.45	0.0	0	0.41	0.0	1	1.89	0.5
Larynx	1	2.78	0.4	6	7.35	0.8	7	4.24	1.7	4	3.59	1.1	18	17.95	1.0
Trachea, bronchus, lung	5	22.46	0.2^b	56	61.09	0.9	42	36.55	1.1	31	33.45	0.9	134	153.45	0.9
Prostate gland	41	25.57	1.6^b	83	71.33	1.2	61	45.03	1.4^b	59	44.37	1.3^b	244	186.18	1.3^b
Testis	0	0.17	0.0	0	0.42	0.0	0	0.23	0.0	0	0.18	0.0	0	0.99	0.0
Kidney, renal pelvis, ureter	5	3.17	1.6	13	8.53	1.5	8	5.10	1.6	11	4.61	2.4^b	37	21.39	1.7^b
Bladder, other urinary	11	9.64	1.1	25	26.50	0.9	20	16.32	1.2	20	15.67	1.3	76	68.09	1.1
Melanoma of the skin	3	1.31	2.3	6	3.55	1.7	4	2.10	1.9	1	1.94	0.5	14	8.89	1.6
Eye	0	0.18	0.0	0	0.47	0.0	1	0.27	3.7	1	0.23	4.3	2	1.15	1.7
Brain, central nervous system	0	1.20	0.0	6	3.18	1.9	4	1.81	2.2	0	1.52	0.0	10	7.71	1.3
Thyroid gland	3	0.31	9.6^b	1	0.83	1.2	2	0.48	4.2	0	0.42	0.0	6	2.03	2.9^b
Bone	0	0.18	0.0	2	0.45	4.4	0	0.26	0.0	0	0.21	0.0	2	1.10	1.8
Connective tissue	2	0.63	3.2	1	1.71	0.6	1	1.04	1.0	3	0.98	3.1	7	4.36	1.6
Lymphatic, hematopoietic system	**8**	**8.57**	**0.9**	**26**	**23.44**	**1.1**	**10**	**14.34**	**0.7**	**21**	**13.54**	**1.6**	**65**	**59.85**	**1.1**
Non-Hodgkin's lymphoma	3	2.69	1.1	9	7.35	1.2	2	4.43	0.5	5	4.09	1.2	19	18.55	1.0
Hodgkin's disease	1	0.56	1.8	1	1.45	0.7	1	0.82	1.2	2	0.69	2.9	5	3.51	1.4
Multiple myeloma	0	1.32	0.0	6	3.65	1.6	2	2.26	0.9	3	2.18	1.4	11	9.42	1.2
Leukemias	4	4.00	1.0	10	11.00	0.9	5	6.81	0.7	11	6.57	1.7	30	28.36	1.1
Chronic lymphocytic	0	1.31	0.0	2	3.64	0.5	1	2.27	0.4	4	2.24	1.8	7	9.45	0.7
Acute nonlymphocytic	2	1.18	1.7	3	3.29	0.9	1	2.06	0.5	6	2.07	2.9^b	12	8.60	1.4

[a] ICD-O codes = 153, 159.0.
[b] $P < .05$.

COLON
FEMALES

TABLE 4E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the colon among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	14,480			10,282			4,627			2,401			14,480		
Person-yr in interval	9,891			26,506			16,840			17,239			70,476		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**141**	**102.71**	**1.4**[b]	**389**	**284.07**	**1.4**[b]	**232**	**194.53**	**1.2**[b]	**316**	**222.87**	**1.4**[b]	**1,078**	**803.67**	**1.3**[b]
All excluding site of initial cancer	**117**	**86.50**	**1.4**[b]	**303**	**238.72**	**1.3**[b]	**167**	**162.38**	**1.0**	**229**	**184.35**	**1.2**[b]	**816**	**671.53**	**1.2**[b]
Buccal cavity, pharynx	**3**	**1.71**	**1.8**	**4**	**4.73**	**0.8**	**5**	**3.20**	**1.6**	**7**	**3.60**	**1.9**	**19**	**13.24**	**1.4**
Lip	0	0.12	0.0	0	0.32	0.0	0	0.23	0.0	1	0.27	3.8	1	0.93	1.1
Tongue	0	0.35	0.0	0	0.97	0.0	3	0.65	4.6	2	0.73	2.7	5	2.70	1.9
Salivary gland	0	0.23	0.0	3	0.62	4.8	0	0.42	0.0	0	0.47	0.0	3	1.74	1.7
Gum, other mouth	2	0.61	3.3	0	1.68	0.0	2	1.16	1.7	2	1.35	1.5	6	4.79	1.3
Pharynx	1	0.35	2.8	1	0.98	1.0	0	0.64	0.0	1	0.68	1.5	3	2.65	1.1
Digestive system	**46**	**34.11**	**1.3**	**159**	**94.85**	**1.7**[b]	**102**	**66.60**	**1.5**[b]	**140**	**78.13**	**1.8**[b]	**447**	**273.52**	**1.6**[b]
Esophagus	2	0.72	2.8	4	2.00	2.0	2	1.38	1.5	2	1.61	1.2	10	5.70	1.8
Stomach	1	4.48	0.2	9	12.16	0.7	9	8.37	1.1	8	9.17	0.9	27	34.15	0.8
Colon	24	16.21	1.5	86	45.35	1.9[b]	65	32.15	2.0[b]	87	38.52	2.3[b]	262	132.14	2.0[b]
Rectum	7	6.29	1.1	36	17.49	2.1[b]	18	12.16	1.5	28	14.11	2.0[b]	89	50.03	1.8[b]
Liver, biliary	3	2.34	1.3	3	6.46	0.5	3	4.52	0.7	8	5.18	1.5	17	18.49	0.9
Pancreas	6	3.42	1.8	11	9.61	1.1	3	6.81	0.4	5	8.21	0.6	25	28.03	0.9
Respiratory system	**4**	**5.93**	**0.7**	**17**	**16.60**	**1.0**	**14**	**11.21**	**1.2**	**7**	**13.22**	**0.5**	**42**	**46.93**	**0.9**
Nasal cavities, sinuses	0	0.17	0.0	1	0.46	2.2	2	0.31	6.5	0	0.33	0.0	3	1.26	2.4
Larynx	0	0.32	0.0	0	0.89	0.0	1	0.59	1.7	0	0.66	0.0	1	2.46	0.4
Trachea, bronchus, lung	4	5.37	0.7	16	15.06	1.1	11	10.18	1.1	7	12.09	0.6	38	42.67	0.9
Female breast	22	25.16	0.9	79	69.24	1.1	50	46.59	1.1	81	52.36	1.5[b]	232	193.23	1.2[b]
Female genital tract	**43**	**15.57**	**2.8**[b]	**83**	**42.10**	**2.0**[b]	**28**	**27.40**	**1.0**	**46**	**28.75**	**1.6**[b]	**200**	**113.76**	**1.8**[b]
Cervix uteri	9	2.89	3.1[b]	8	7.52	1.1	4	4.63	0.9	2	4.36	0.5	23	19.38	1.2
Corpus uteri	8	6.22	1.3	31	17.14	1.8[b]	13	11.32	1.1	28	12.33	2.3[b]	80	46.97	1.7[b]
Uterus, NOS	3	1.18	2.6	1	2.99	0.3	1	1.85	0.5	6	1.60	3.8[b]	11	7.61	1.4
Ovary, fallopian tubes	22	4.26	5.2[b]	39	11.61	3.4[b]	7	7.61	0.9	9	8.14	1.1	77	31.60	2.4[b]
Kidney, renal pelvis, ureter	3	1.63	1.8	2	4.54	0.4	2	3.12	0.6	4	3.57	1.1	11	12.86	0.9
Bladder, other urinary	8	3.10	2.6[b]	12	8.73	1.4	1	6.25	0.2[b]	4	7.62	0.5	25	25.69	1.0
Melanoma of the skin	4	1.03	3.9[b]	1	2.86	0.3	4	1.91	2.1	1	2.19	0.5	10	7.98	1.3
Eye	0	0.17	0.0	0	0.47	0.0	2	0.32	6.2	0	0.35	0.0	2	1.32	1.5
Brain, central nervous system	1	0.92	1.1	4	2.53	1.6	3	1.64	1.8	5	1.77	2.8	13	6.87	1.9[b]
Thyroid gland	0	0.66	0.0	1	1.81	0.6	0	1.20	0.0	2	1.30	1.5	3	4.96	0.6
Bone	0	0.15	0.0	1	0.39	2.6	0	0.25	0.0	0	0.25	0.0	1	1.04	1.0
Connective tissue	1	0.43	2.4	1	1.17	0.9	2	0.80	2.5	0	0.90	0.0	4	3.30	1.2
Lymphatic, hematopoietic system	**6**	**6.91**	**0.9**	**20**	**19.45**	**1.0**	**16**	**13.69**	**1.2**	**15**	**16.57**	**0.9**	**57**	**56.59**	**1.0**
Non-Hodgkin's lymphoma	4	2.54	1.6	6	7.12	0.8	4	4.94	0.8	9	5.90	1.5	23	20.48	1.1
Hodgkin's disease	0	0.44	0.0	1	1.19	0.8	1	0.79	1.3	1	0.85	1.2	3	3.26	0.9
Multiple myeloma	1	1.23	0.8	4	3.51	1.1	3	2.51	1.2	2	3.15	0.6	10	10.40	1.0
Leukemias	1	2.69	0.4	9	7.59	1.2	8	5.44	1.5	3	6.66	0.5	21	22.38	0.9
Chronic lymphocytic	1	0.78	1.3	3	2.22	1.3	2	1.63	1.2	0	2.05	0.0	6	6.69	0.9
Acute nonlymphocytic	0	0.88	0.0	3	2.51	1.2	3	1.81	1.7	2	2.30	0.9	8	7.50	1.1

[a] ICD-O codes = 153, 159.0.

[b] $P < .05$.

RECTUM
BOTH SEXES

TABLE 5A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the rectum, rectosigmoid junction, or anus, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	8,557	6,903	15,460
No. who developed a second primary cancer	582	370	952
Average age at diagnosis of first cancer, yr	64	65	65
Average yr of diagnosis of first cancer	1964	1964	1964
Person-yr of follow-up	35,009	33,660	68,668
Average follow-up, yr	4.1	4.9	4.4
Percent given radiotherapy for first cancer	10.2	9.0	9.6

[a] ICD-O code = 154.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 5B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the rectum, rectosigmoid junction, or anus in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	847	89.0
Only the first cancer	87	9.2
Only the second cancer	13	1.4
Neither first nor second cancer	5	0.5
Total second primary cancers	952	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

RECTUM
BOTH SEXES

TABLE 5C. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the rectum, rectosigmoid junction, or anus among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	15,460			11,091			4,382			2,172			15,460		
Person-yr in interval	10,733			27,049			15,642			15,245			68,668		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**122**	**129.45**	**0.9**	**320**	**341.80**	**0.9**	**217**	**220.84**	**1.0**	**293**	**249.42**	**1.2**[b]	**952**	**940.91**	**1.0**
All excluding site of initial cancer	**119**	**120.98**	**1.0**	**310**	**319.78**	**1.0**	**215**	**206.78**	**1.0**	**287**	**233.79**	**1.2**[b]	**931**	**880.76**	**1.1**
Buccal cavity, pharynx	**1**	**5.03**	**0.2**	**9**	**12.83**	**0.7**	**9**	**7.74**	**1.2**	**8**	**7.67**	**1.0**	**27**	**33.24**	**0.8**
Lip	0	0.87	0.0	0	2.11	0.0	2	1.26	1.6	1	1.20	0.8	3	5.43	0.6
Tongue	0	1.00	0.0	2	2.55	0.8	1	1.52	0.7	1	1.49	0.7	4	6.56	0.6
Salivary gland	1	0.31	3.2	0	0.82	0.0	0	0.52	0.0	2	0.59	3.4	3	2.25	1.3
Gum, other mouth	0	1.44	0.0	3	3.71	0.8	5	2.27	2.2	3	2.29	1.3	11	9.71	1.1
Pharynx	0	1.20	0.0	3	3.12	1.0	1	1.87	0.5	1	1.81	0.6	5	8.00	0.6
Digestive system	**38**	**42.15**	**0.9**	**98**	**109.94**	**0.9**	**77**	**71.25**	**1.1**	**114**	**81.26**	**1.4**[b]	**327**	**304.42**	**1.1**
Esophagus	2	2.15	0.9	5	5.47	0.9	2	3.32	0.6	5	3.30	1.5	14	14.23	1.0
Stomach	5	7.22	0.7	10	17.91	0.6	7	11.08	0.6	12	11.66	1.0	34	47.84	0.7[b]
Colon	25	16.92	1.5	60	45.16	1.3[b]	57	30.16	1.9[b]	80	36.17	2.2[b]	222	128.33	1.7[b]
Rectum	3	8.47	0.4	10	22.02	0.5[b]	2	14.06	0.1[b]	6	15.63	0.4[b]	21	60.15	0.3[b]
Liver, biliary	0	2.42	0.0	7	6.31	1.1	2	4.12	0.5	4	4.75	0.8	13	17.58	0.7
Pancreas	3	4.21	0.7	4	11.12	0.4[b]	6	7.29	0.8	6	8.41	0.7	19	31.01	0.6[b]
Respiratory system	**12**	**19.01**	**0.6**	**40**	**50.84**	**0.8**	**39**	**32.12**	**1.2**	**32**	**33.95**	**0.9**	**123**	**135.84**	**0.9**
Nasal cavities, sinuses	0	0.26	0.0	0	0.67	0.0	0	0.42	0.0	2	0.45	4.4	2	1.81	1.1
Larynx	2	2.02	1.0	5	5.22	1.0	4	3.12	1.3	3	2.98	1.0	14	13.34	1.0
Trachea, bronchus, lung	10	16.54	0.6	35	44.47	0.8	35	28.29	1.2	27	30.20	0.9	107	119.43	0.9
Female breast	10	11.70	0.9	30	31.66	0.9	12	20.68	0.6	39	24.78	1.6[b]	91	88.77	1.0
Female genital tract	**10**	**7.51**	**1.3**	**21**	**19.92**	**1.1**	**13**	**12.54**	**1.0**	**18**	**13.97**	**1.3**	**62**	**53.91**	**1.2**
Cervix uteri	1	1.48	0.7	1	3.71	0.3	4	2.19	1.8	3	2.16	1.4	9	9.53	0.9
Corpus uteri	2	2.94	0.7	10	8.10	1.2	5	5.21	1.0	5	6.02	0.8	22	22.26	1.0
Uterus, NOS	1	0.61	1.6	1	1.46	0.7	0	0.85	0.0	1	0.75	1.3	3	3.67	0.8
Ovary, fallopian tubes	6	2.02	3.0[b]	8	5.42	1.5	2	3.46	0.6	6	3.96	1.5	22	14.85	1.5
Prostate gland	27	15.06	1.8[b]	56	39.83	1.4[b]	32	26.76	1.2	33	31.09	1.1	148	112.67	1.3[b]
Testis	1	0.12	8.2	0	0.29	0.0	0	0.15	0.0	0	0.12	0.0	1	0.69	1.5
Kidney, renal pelvis, ureter	4	2.76	1.5	7	7.29	1.0	2	4.65	0.4	3	5.02	0.6	16	19.71	0.8
Bladder, other urinary	8	7.26	1.1	28	19.27	1.5	8	12.65	0.6	16	14.55	1.1	60	53.69	1.1
Melanoma of the skin	1	1.32	0.8	1	3.49	0.3	0	2.18	0.0	3	2.42	1.2	5	9.39	0.5
Eye	2	0.20	9.9[b]	0	0.52	0.0	0	0.32	0.0	0	0.34	0.0	2	1.38	1.4
Brain, central nervous system	0	1.25	0.0	3	3.32	0.9	0	2.00	0.0	1	2.02	0.5	4	8.58	0.5
Thyroid gland	0	0.51	0.0	0	1.36	0.0	1	0.85	1.2	1	0.92	1.1	2	3.63	0.6
Bone	0	0.20	0.0	1	0.48	2.1	0	0.28	0.0	0	0.27	0.0	1	1.23	0.8
Connective tissue	0	0.60	0.0	2	1.55	1.3	2	0.98	2.0	0	1.11	0.0	4	4.24	0.9
Lymphatic, hematopoietic system	**5**	**8.36**	**0.6**	**22**	**22.37**	**1.0**	**17**	**14.73**	**1.2**	**20**	**17.30**	**1.2**	**64**	**62.71**	**1.0**
Non-Hodgkin's lymphoma	3	2.82	1.1	4	7.59	0.5	2	4.94	0.4	7	5.70	1.2	16	21.04	0.8
Hodgkin's disease	0	0.58	0.0	1	1.49	0.7	1	0.90	1.1	0	0.91	0.0	2	3.88	0.5
Multiple myeloma	1	1.33	0.8	7	3.65	1.9	4	2.45	1.6	4	3.02	1.3	16	10.44	1.5
Leukemias	1	3.61	0.3	10	9.61	1.0	10	6.43	1.6	9	7.67	1.2	30	27.30	1.1
Chronic lymphocytic	0	1.12	0.0	1	3.01	0.3	5	2.04	2.4	1	2.51	0.4	7	8.67	0.8
Acute nonlymphocytic	1	1.07	0.9	4	2.94	1.4	2	2.00	1.0	3	2.50	1.2	10	8.51	1.2

[a] ICD-O code = 154.

[b] $P < .05$.

RECTUM
MALES

TABLE 5D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the rectum, rectosigmoid junction, or anus among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	8,557			6,018			2,265			1,073			8,557		
Person-yr in interval	5,885			14,362			7,890			6,871			35,008		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**75**	**82.57**	**0.9**	**214**	**214.48**	**1.0**	**133**	**136.05**	**1.0**	**160**	**144.93**	**1.1**	**582**	**577.65**	**1.0**
All excluding site of initial cancer	**75**	**76.95**	**1.0**	**205**	**200.19**	**1.0**	**131**	**127.21**	**1.0**	**157**	**135.86**	**1.2**	**568**	**539.85**	**1.1**
Buccal cavity, pharynx	**1**	**4.24**	**0.2**	**8**	**10.65**	**0.8**	**8**	**6.32**	**1.3**	**7**	**5.96**	**1.2**	**24**	**27.15**	**0.9**
Lip	0	0.81	0.0	0	1.97	0.0	2	1.16	1.7	1	1.08	0.9	3	5.02	0.6
Tongue	0	0.84	0.0	2	2.10	1.0	1	1.24	0.8	1	1.14	0.9	4	5.32	0.8
Salivary gland	1	0.21	4.8	0	0.55	0.0	0	0.34	0.0	2	0.37	5.4	3	1.47	2.0
Gum, other mouth	0	1.17	0.0	3	2.95	1.0	5	1.76	2.8	2	1.66	1.2	10	7.54	1.3
Pharynx	0	1.03	0.0	2	2.65	0.8	0	1.58	0.0	1	1.48	0.7	3	6.74	0.4
Digestive system	**21**	**26.98**	**0.8**	**64**	**68.75**	**0.9**	**44**	**43.06**	**1.0**	**63**	**45.23**	**1.4**[b]	**192**	**183.90**	**1.0**
Esophagus	1	1.82	0.6	5	4.58	1.1	1	2.73	0.4	5	2.56	2.0	12	11.68	1.0
Stomach	4	5.16	0.8	5	12.53	0.4[b]	2	7.52	0.3[b]	6	7.46	0.8	17	32.65	0.5[b]
Colon	14	9.85	1.4	38	25.70	1.5[b]	34	16.64	2.0[b]	43	18.43	2.3[b]	129	70.58	1.8[b]
Rectum	0	5.62	0.0[b]	9	14.29	0.6	2	8.84	0.2[b]	3	9.07	0.3[b]	14	37.80	0.4[b]
Liver, biliary	0	1.37	0.0	2	3.50	0.6	1	2.21	0.5	1	2.37	0.4	4	9.44	0.4
Pancreas	2	2.71	0.7	4	6.98	0.6	4	4.41	0.9	4	4.63	0.9	14	18.72	0.7
Respiratory system	**10**	**16.30**	**0.6**	**32**	**43.23**	**0.7**	**31**	**27.06**	**1.1**	**25**	**27.67**	**0.9**	**98**	**114.18**	**0.9**
Nasal cavities, sinuses	0	0.18	0.0	0	0.46	0.0	0	0.28	0.0	1	0.29	3.4	1	1.22	0.8
Larynx	2	1.87	1.1	5	4.80	1.0	4	2.84	1.4	3	2.66	1.1	14	12.17	1.2
Trachea, bronchus, lung	8	14.10	0.6	27	37.58	0.7	27	23.70	1.1	21	24.47	0.9	83	99.78	0.8
Prostate gland	27	15.06	1.8[b]	56	39.83	1.4[b]	32	26.76	1.2	33	31.09	1.1	148	112.67	1.3[b]
Testis	1	0.12	8.2	0	0.29	0.0	0	0.15	0.0	0	0.12	0.0	1	0.69	1.5
Kidney, renal pelvis, ureter	3	2.02	1.5	6	5.28	1.1	1	3.28	0.3	1	3.33	0.3	11	13.89	0.8
Bladder, other urinary	7	5.90	1.2	26	15.54	1.7[b]	6	10.04	0.6	12	11.08	1.1	51	42.53	1.2
Melanoma of the skin	1	0.83	1.2	0	2.17	0.0	0	1.33	0.0	2	1.38	1.4	3	5.71	0.5
Eye	0	0.12	0.0	0	0.31	0.0	0	0.18	0.0	0	0.17	0.0	0	0.78	0.0
Brain, central nervous system	0	0.82	0.0	3	2.12	1.4	0	1.23	0.0	0	1.13	0.0	3	5.30	0.6
Thyroid gland	0	0.21	0.0	0	0.53	0.0	0	0.32	0.0	1	0.30	3.4	1	1.35	0.7
Bone	0	0.13	0.0	1	0.30	3.3	0	0.17	0.0	0	0.15	0.0	1	0.75	1.3
Connective tissue	0	0.40	0.0	2	1.02	2.0	1	0.64	1.6	0	0.69	0.0	3	2.75	1.1
Lymphatic, hematopoietic system	**3**	**5.32**	**0.6**	**14**	**13.94**	**1.0**	**8**	**8.90**	**0.9**	**12**	**9.63**	**1.2**	**37**	**37.76**	**1.0**
Non-Hodgkin's lymphoma	1	1.70	0.6	3	4.46	0.7	0	2.80	0.0	4	2.94	1.4	8	11.90	0.7
Hodgkin's disease	0	0.38	0.0	1	0.95	1.1	0	0.54	0.0	0	0.50	0.0	1	2.37	0.4
Multiple myeloma	1	0.80	1.2	4	2.15	1.9	1	1.40	0.7	2	1.55	1.3	8	5.90	1.4
Leukemias	1	2.44	0.4	6	6.38	0.9	7	4.16	1.7	6	4.63	1.3	20	17.60	1.1
Chronic lymphocytic	0	0.79	0.0	1	2.08	0.5	2	1.37	1.5	1	1.57	0.6	4	5.80	0.7
Acute nonlymphocytic	1	0.69	1.4	2	1.87	1.1	2	1.25	1.6	2	1.46	1.4	7	5.26	1.3

[a] ICD-O code = 154.

[b] $P < .05$.

RECTUM
FEMALES

TABLE 5E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the rectum, rectosigmoid junction, or anus among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,903			5,073			2,117			1,099			6,903		
Person-yr in interval	4,847			12,686			7,752			8,375			33,660		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**47**	**46.89**	**1.0**	**106**	**127.32**	**0.8**	**84**	**84.80**	**1.0**	**133**	**104.48**	**1.3**[b]	**370**	**363.25**	**1.0**
All excluding site of initial cancer	**44**	**44.04**	**1.0**	**105**	**119.59**	**0.9**	**84**	**79.58**	**1.1**	**130**	**97.92**	**1.3**[b]	**363**	**340.90**	**1.1**
Buccal cavity, pharynx	**0**	**0.79**	**0.0**	**1**	**2.18**	**0.5**	**1**	**1.42**	**0.7**	**1**	**1.71**	**0.6**	**3**	**6.09**	**0.5**
Lip	0	0.05	0.0	0	0.14	0.0	0	0.10	0.0	0	0.12	0.0	0	0.41	0.0
Tongue	0	0.16	0.0	0	0.45	0.0	0	0.29	0.0	0	0.35	0.0	0	1.25	0.0
Salivary gland	0	0.10	0.0	0	0.28	0.0	0	0.18	0.0	0	0.23	0.0	0	0.79	0.0
Gum, other mouth	0	0.28	0.0	0	0.76	0.0	0	0.51	0.0	1	0.63	1.6	1	2.18	0.5
Pharynx	0	0.17	0.0	1	0.47	2.1	1	0.30	3.4	0	0.33	0.0	2	1.26	1.6
Digestive system	**17**	**15.17**	**1.1**	**34**	**41.19**	**0.8**	**33**	**28.20**	**1.2**	**51**	**36.03**	**1.4**[b]	**135**	**120.52**	**1.1**
Esophagus	1	0.33	3.0	0	0.89	0.0	1	0.59	1.7	0	0.74	0.0	2	2.55	0.8
Stomach	1	2.07	0.5	5	5.37	0.9	5	3.56	1.4	6	4.21	1.4	17	15.19	1.1
Colon	11	7.07	1.6	22	19.46	1.1	23	13.52	1.7[b]	37	17.74	2.1[b]	93	57.75	1.6[b]
Rectum	3	2.85	1.1	1	7.73	0.1[b]	0	5.22	0.0[b]	3	6.56	0.5	7	22.35	0.3[b]
Liver, biliary	0	1.05	0.0	5	2.81	1.8	1	1.90	0.5	3	2.38	1.3	9	8.14	1.1
Pancreas	1	1.50	0.7	0	4.13	0.0[b]	2	2.88	0.7	2	3.78	0.5	5	12.29	0.4[b]
Respiratory system	**2**	**2.71**	**0.7**	**8**	**7.62**	**1.1**	**8**	**5.06**	**1.6**	**7**	**6.28**	**1.1**	**25**	**21.66**	**1.2**
Nasal cavities, sinuses	0	0.08	0.0	0	0.21	0.0	0	0.14	0.0	1	0.16	6.3	1	0.59	1.7
Larynx	0	0.15	0.0	0	0.42	0.0	0	0.27	0.0	0	0.32	0.0	0	1.17	0.0
Trachea, bronchus, lung	2	2.44	0.8	8	6.89	1.2	8	4.59	1.7	6	5.74	1.0	24	19.65	1.2
Female breast	10	11.70	0.9	30	31.66	0.9	12	20.68	0.6	39	24.78	1.6[b]	91	88.77	1.0
Female genital tract	**10**	**7.51**	**1.3**	**21**	**19.92**	**1.1**	**13**	**12.54**	**1.0**	**18**	**13.97**	**1.3**	**62**	**53.91**	**1.2**
Cervix uteri	1	1.48	0.7	1	3.71	0.3	4	2.19	1.8	3	2.16	1.4	9	9.53	0.9
Corpus uteri	2	2.94	0.7	10	8.10	1.2	5	5.21	1.0	5	6.02	0.8	22	22.26	1.0
Uterus, NOS	1	0.61	1.6	1	1.46	0.7	0	0.85	0.0	1	0.75	1.3	3	3.67	0.8
Ovary, fallopian tubes	6	2.02	3.0[b]	8	5.42	1.5	2	3.46	0.6	6	3.96	1.5	22	14.85	1.5
Kidney, renal pelvis, ureter	1	0.73	1.4	1	2.02	0.5	1	1.38	0.7	2	1.69	1.2	5	5.82	0.9
Bladder, other urinary	1	1.36	0.7	2	3.74	0.5	2	2.61	0.8	4	3.47	1.2	9	11.16	0.8
Melanoma of the skin	0	0.48	0.0	1	1.31	0.8	0	0.85	0.0	1	1.04	1.0	2	3.68	0.5
Eye	2	0.08	24.8[b]	0	0.21	0.0	0	0.14	0.0	0	0.17	0.0	2	0.61	3.3
Brain, central nervous system	0	0.43	0.0	0	1.20	0.0	0	0.77	0.0	1	0.88	1.1	1	3.29	0.3
Thyroid gland	0	0.31	0.0	0	0.82	0.0	1	0.53	1.9	0	0.62	0.0	1	2.28	0.4
Bone	0	0.07	0.0	0	0.18	0.0	0	0.11	0.0	0	0.12	0.0	0	0.49	0.0
Connective tissue	0	0.20	0.0	0	0.53	0.0	1	0.34	2.9	0	0.42	0.0	1	1.49	0.7
Lymphatic, hematopoietic system	**2**	**3.03**	**0.7**	**8**	**8.43**	**0.9**	**9**	**5.83**	**1.5**	**8**	**7.67**	**1.0**	**27**	**24.95**	**1.1**
Non-Hodgkin's lymphoma	2	1.12	1.8	1	3.13	0.3	2	2.14	0.9	3	2.75	1.1	8	9.15	0.9
Hodgkin's disease	0	0.20	0.0	0	0.55	0.0	1	0.35	2.8	0	0.41	0.0	1	1.51	0.7
Multiple myeloma	0	0.53	0.0	3	1.50	2.0	3	1.06	2.8	2	1.46	1.4	8	4.54	1.8
Leukemias	0	1.17	0.0	4	3.23	1.2	3	2.27	1.3	3	3.04	1.0	10	9.71	1.0
Chronic lymphocytic	0	0.33	0.0	0	0.92	0.0	3	0.67	4.5	0	0.94	0.0	3	2.87	1.0
Acute nonlymphocytic	0	0.38	0.0	2	1.07	1.9	0	0.75	0.0	1	1.04	1.0	3	3.24	0.9

[a] ICD-O code = 154.

[b] $P < .05$.

LIVER,
BILIARY
BOTH SEXES

TABLE 6A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the liver, gallbladder, or other biliary, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,165	1,580	2,745
No. who developed a second primary cancer	26	21	47
Average age at diagnosis of first cancer, yr	65	66	66
Average yr of diagnosis of first cancer	1967	1964	1965
Person-yr of follow-up	1,198	1,962	3,160
Average follow-up, yr	1.0	1.2	1.2
Percent given radiotherapy for first cancer	11.0	7.5	9.0

[a] ICD-O codes = 155–156.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 6B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the liver, gallbladder, or other biliary in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	41	87.2
Only the first cancer	5	10.6
Only the second cancer	1	2.1
Neither first nor second cancer	0	0.0
Total second primary cancers	47	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LIVER,
BILIARY
BOTH SEXES

TABLE 6C. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the liver, gallbladder, or other biliary among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,745			716			156			75			2,745		
Person-yr in interval	1,022			1,160			518			461			3,160		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**16**	**12.37**	**1.3**	**19**	**13.98**	**1.4**	**6**	**6.49**	**0.9**	**6**	**7.19**	**0.8**	**47**	**40.00**	**1.2**
All excluding site of initial cancer	**16**	**12.12**	**1.3**	**18**	**13.71**	**1.3**	**5**	**6.37**	**0.8**	**6**	**7.06**	**0.8**	**45**	**39.23**	**1.1**
Buccal cavity, pharynx	**0**	**0.41**	**0.0**	**0**	**0.45**	**0.0**	**0**	**0.19**	**0.0**	**0**	**0.19**	**0.0**	**0**	**1.24**	**0.0**
Lip	0	0.06	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.18	0.0
Tongue	0	0.08	0.0	0	0.09	0.0	0	0.04	0.0	0	0.04	0.0	0	0.25	0.0
Salivary gland	0	0.03	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Gum, other mouth	0	0.12	0.0	0	0.13	0.0	0	0.06	0.0	0	0.06	0.0	0	0.38	0.0
Pharynx	0	0.10	0.0	0	0.11	0.0	0	0.04	0.0	0	0.05	0.0	0	0.30	0.0
Digestive system	**6**	**4.01**	**1.5**	**12**	**4.49**	**2.7**[b]	**4**	**2.10**	**1.9**	**2**	**2.29**	**0.9**	**24**	**12.87**	**1.9**[b]
Esophagus	0	0.17	0.0	0	0.19	0.0	0	0.08	0.0	0	0.08	0.0	0	0.52	0.0
Stomach	0	0.63	0.0	0	0.66	0.0	0	0.29	0.0	0	0.29	0.0	0	1.87	0.0
Colon	3	1.69	1.8	3	1.94	1.5	2	0.94	2.1	1	1.06	0.9	9	5.63	1.6
Rectum	0	0.79	0.0	5	0.89	5.6[b]	0	0.41	0.0	0	0.44	0.0	5	2.53	2.0
Liver, biliary	0	0.25	0.0	1	0.27	3.7	1	0.12	8.1	0	0.13	0.0	2	0.77	2.6
Pancreas	2	0.41	4.9	3	0.46	6.5[b]	1	0.22	4.5	1	0.24	4.2	7	1.33	5.3[b]
Respiratory system	**0**	**1.66**	**0.0**	**2**	**1.85**	**1.1**	**1**	**0.77**	**1.3**	**1**	**0.93**	**1.1**	**4**	**5.20**	**0.8**
Nasal cavities, sinuses	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Larynx	0	0.16	0.0	0	0.18	0.0	0	0.07	0.0	0	0.07	0.0	0	0.48	0.0
Trachea, bronchus, lung	0	1.46	0.0	2	1.62	1.2	1	0.68	1.5	1	0.84	1.2	4	4.60	0.9
Female breast	1	1.47	0.7	0	1.80	0.0	0	0.95	0.0	2	0.88	2.3	3	5.09	0.6
Female genital tract	**1**	**0.93**	**1.1**	**1**	**1.12**	**0.9**	**0**	**0.57**	**0.0**	**0**	**0.49**	**0.0**	**2**	**3.10**	**0.6**
Cervix uteri	0	0.18	0.0	1	0.20	5.0	0	0.09	0.0	0	0.07	0.0	1	0.54	1.8
Corpus uteri	0	0.36	0.0	0	0.46	0.0	0	0.24	0.0	0	0.22	0.0	0	1.29	0.0
Uterus, NOS	0	0.08	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.21	0.0
Ovary, fallopian tubes	1	0.25	4.0	0	0.31	0.0	0	0.16	0.0	0	0.14	0.0	1	0.86	1.2
Prostate gland	5	1.17	4.3[b]	2	1.21	1.7	0	0.50	0.0	1	0.78	1.3	8	3.66	2.2
Testis	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Kidney, renal pelvis, ureter	1	0.26	3.9	0	0.28	0.0	0	0.13	0.0	0	0.14	0.0	1	0.81	1.2
Bladder, other urinary	1	0.64	1.6	0	0.71	0.0	1	0.31	3.2	0	0.40	0.0	2	2.06	1.0
Melanoma of the skin	0	0.13	0.0	0	0.15	0.0	0	0.06	0.0	0	0.08	0.0	0	0.42	0.0
Eye	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Brain, central nervous system	0	0.12	0.0	0	0.14	0.0	0	0.06	0.0	0	0.06	0.0	0	0.38	0.0
Thyroid gland	0	0.05	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.18	0.0
Bone	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.06	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.17	0.0
Lymphatic, hematopoietic system	**1**	**0.81**	**1.2**	**2**	**0.93**	**2.1**	**0**	**0.45**	**0.0**	**0**	**0.51**	**0.0**	**3**	**2.70**	**1.1**
Non-Hodgkin's lymphoma	0	0.28	0.0	0	0.32	0.0	0	0.15	0.0	0	0.17	0.0	0	0.93	0.0
Hodgkin's disease	0	0.05	0.0	1	0.06	16.2	0	0.03	0.0	0	0.03	0.0	1	0.17	5.9
Multiple myeloma	0	0.13	0.0	1	0.16	6.3	0	0.08	0.0	0	0.09	0.0	1	0.46	2.2
Leukemias	1	0.34	2.9	0	0.39	0.0	0	0.19	0.0	0	0.22	0.0	1	1.14	0.9
Chronic lymphocytic	0	0.11	0.0	0	0.12	0.0	0	0.06	0.0	0	0.07	0.0	0	0.36	0.0
Acute nonlymphocytic	0	0.11	0.0	0	0.12	0.0	0	0.06	0.0	0	0.08	0.0	0	0.37	0.0

[a] ICD-O codes = 155–156.

[b] $P < .05$.

LIVER, BILIARY MALES

TABLE 6D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the liver, gallbladder, or other biliary among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,165			309			55			23			1,165		
Person-yr in interval	432			449			161			156			1,198		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**10**	**6.38**	**1.6**	**10**	**6.69**	**1.5**	**3**	**2.64**	**1.1**	**3**	**3.52**	**0.9**	**26**	**19.21**	**1.4**
All excluding site of initial cancer	**10**	**6.27**	**1.6**	**9**	**6.58**	**1.4**	**2**	**2.60**	**0.8**	**3**	**3.47**	**0.9**	**24**	**18.90**	**1.3**
Buccal cavity, pharynx	**0**	**0.31**	**0.0**	**0**	**0.32**	**0.0**	**0**	**0.13**	**0.0**	**0**	**0.13**	**0.0**	**0**	**0.89**	**0.0**
Lip	0	0.06	0.0	0	0.06	0.0	0	0.02	0.0	0	0.02	0.0	0	0.15	0.0
Tongue	0	0.06	0.0	0	0.06	0.0	0	0.02	0.0	0	0.02	0.0	0	0.17	0.0
Salivary gland	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Gum, other mouth	0	0.09	0.0	0	0.09	0.0	0	0.04	0.0	0	0.04	0.0	0	0.25	0.0
Pharynx	0	0.08	0.0	0	0.08	0.0	0	0.03	0.0	0	0.03	0.0	0	0.23	0.0
Digestive system	**2**	**2.01**	**1.0**	**6**	**2.09**	**2.9**[b]	**1**	**0.84**	**1.2**	**2**	**1.06**	**1.9**	**11**	**5.99**	**1.8**
Esophagus	0	0.13	0.0	0	0.14	0.0	0	0.05	0.0	0	0.06	0.0	0	0.37	0.0
Stomach	0	0.35	0.0	0	0.35	0.0	0	0.15	0.0	0	0.16	0.0	0	1.01	0.0
Colon	0	0.76	0.0	3	0.80	3.8	0	0.32	0.0	1	0.46	2.2	4	2.33	1.7
Rectum	0	0.42	0.0	0	0.44	0.0	0	0.17	0.0	0	0.21	0.0	0	1.25	0.0
Liver, biliary	0	0.11	0.0	1	0.11	9.4	1	0.04	24.0	0	0.05	0.0	2	0.31	6.5
Pancreas	2	0.21	9.7[b]	2	0.22	9.2[b]	0	0.09	0.0	1	0.11	9.1	5	0.62	8.1[b]
Respiratory system	**0**	**1.33**	**0.0**	**1**	**1.43**	**0.7**	**1**	**0.53**	**1.9**	**0**	**0.69**	**0.0**	**2**	**3.98**	**0.5**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.14	0.0	0	0.16	0.0	0	0.06	0.0	0	0.06	0.0	0	0.42	0.0
Trachea, bronchus, lung	0	1.16	0.0	1	1.25	0.8	1	0.47	2.1	0	0.62	0.0	2	3.49	0.6
Prostate gland	5	1.17	4.3[b]	2	1.21	1.7	0	0.50	0.0	1	0.78	1.3	8	3.66	2.2
Testis	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Kidney, renal pelvis, ureter	1	0.16	6.3	0	0.17	0.0	0	0.07	0.0	0	0.08	0.0	1	0.48	2.1
Bladder, other urinary	1	0.46	2.2	0	0.49	0.0	1	0.19	5.2	0	0.28	0.0	2	1.42	1.4
Melanoma of the skin	0	0.07	0.0	0	0.07	0.0	0	0.03	0.0	0	0.04	0.0	0	0.20	0.0
Eye	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Brain, central nervous system	0	0.07	0.0	0	0.07	0.0	0	0.02	0.0	0	0.03	0.0	0	0.19	0.0
Thyroid gland	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Connective tissue	0	0.03	0.0	0	0.03	0.0	0	0.01	0.0	0	0.02	0.0	0	0.09	0.0
Lymphatic, hematopoietic system	**1**	**0.42**	**2.4**	**1**	**0.44**	**2.3**	**0**	**0.18**	**0.0**	**0**	**0.24**	**0.0**	**2**	**1.27**	**1.6**
Non-Hodgkin's lymphoma	0	0.13	0.0	0	0.14	0.0	0	0.05	0.0	0	0.07	0.0	0	0.40	0.0
Hodgkin's disease	0	0.03	0.0	1	0.03	33.9	0	0.01	0.0	0	0.01	0.0	1	0.08	12.4
Multiple myeloma	0	0.06	0.0	0	0.07	0.0	0	0.03	0.0	0	0.04	0.0	0	0.20	0.0
Leukemias	1	0.19	5.3	0	0.19	0.0	0	0.08	0.0	0	0.11	0.0	1	0.58	1.7
Chronic lymphocytic	0	0.06	0.0	0	0.06	0.0	0	0.03	0.0	0	0.04	0.0	0	0.19	0.0
Acute nonlymphocytic	0	0.06	0.0	0	0.06	0.0	0	0.03	0.0	0	0.04	0.0	0	0.18	0.0

[a] ICD-O codes = 155–156.

[b] $P < .05$.

LIVER, BILIARY FEMALES

TABLE 6E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the liver, gallbladder, or other biliary among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,580			407			101			52			1,580		
Person-yr in interval	589			711			357			305			1,962		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	6	5.99	1.0	9	7.29	1.2	3	3.85	0.8	3	3.67	0.8	21	20.79	1.0
All excluding site of initial cancer	6	5.85	1.0	9	7.13	1.3	3	3.77	0.8	3	3.59	0.8	21	20.32	1.0
Buccal cavity, pharynx	0	0.10	0.0	0	0.12	0.0	0	0.06	0.0	0	0.06	0.0	0	0.35	0.0
Lip	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Tongue	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Gum, other mouth	0	0.04	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.12	0.0
Pharynx	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Digestive system	4	1.99	2.0	6	2.40	2.5	3	1.26	2.4	0	1.23	0.0	13	6.88	1.9^b
Esophagus	0	0.04	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.15	0.0
Stomach	0	0.27	0.0	0	0.31	0.0	0	0.15	0.0	0	0.13	0.0	0	0.86	0.0
Colon	3	0.93	3.2	0	1.14	0.0	2	0.62	3.2	0	0.61	0.0	5	3.29	1.5
Rectum	0	0.37	0.0	5	0.45	11.2^b	0	0.24	0.0	0	0.23	0.0	5	1.28	3.9^b
Liver, biliary	0	0.14	0.0	0	0.16	0.0	0	0.08	0.0	0	0.08	0.0	0	0.47	0.0
Pancreas	0	0.20	0.0	1	0.24	4.1	1	0.13	7.5	0	0.13	0.0	2	0.71	2.8
Respiratory system	0	0.34	0.0	1	0.41	2.4	0	0.23	0.0	1	0.24	4.2	2	1.22	1.6
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.03	0.0
Larynx	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Trachea, bronchus, lung	0	0.30	0.0	1	0.37	2.7	0	0.21	0.0	1	0.22	4.6	2	1.11	1.8
Female breast	1	1.47	0.7	0	1.80	0.0	0	0.95	0.0	2	0.88	2.3	3	5.09	0.6
Female genital tract	1	0.93	1.1	1	1.12	0.9	0	0.57	0.0	0	0.49	0.0	2	3.10	0.6
Cervix uteri	0	0.18	0.0	1	0.20	5.0	0	0.09	0.0	0	0.07	0.0	1	0.54	1.8
Corpus uteri	0	0.36	0.0	0	0.46	0.0	0	0.24	0.0	0	0.22	0.0	0	1.29	0.0
Uterus, NOS	0	0.08	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.21	0.0
Ovary, fallopian tubes	1	0.25	4.0	0	0.31	0.0	0	0.16	0.0	0	0.14	0.0	1	0.86	1.2
Kidney, renal pelvis, ureter	0	0.10	0.0	0	0.11	0.0	0	0.06	0.0	0	0.06	0.0	0	0.33	0.0
Bladder, other urinary	0	0.18	0.0	0	0.22	0.0	0	0.12	0.0	0	0.12	0.0	0	0.64	0.0
Melanoma of the skin	0	0.06	0.0	0	0.08	0.0	0	0.04	0.0	0	0.04	0.0	0	0.21	0.0
Eye	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Brain, central nervous system	0	0.05	0.0	0	0.07	0.0	0	0.04	0.0	0	0.03	0.0	0	0.19	0.0
Thyroid gland	0	0.04	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.13	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Connective tissue	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.08	0.0
Lymphatic, hematopoietic system	0	0.39	0.0	1	0.50	2.0	0	0.27	0.0	0	0.27	0.0	1	1.43	0.7
Non-Hodgkin's lymphoma	0	0.14	0.0	0	0.18	0.0	0	0.10	0.0	0	0.10	0.0	0	0.52	0.0
Hodgkin's disease	0	0.03	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Multiple myeloma	0	0.07	0.0	1	0.09	11.1	0	0.05	0.0	0	0.05	0.0	1	0.26	3.8
Leukemias	0	0.15	0.0	0	0.19	0.0	0	0.10	0.0	0	0.11	0.0	0	0.56	0.0
Chronic lymphocytic	0	0.04	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.17	0.0
Acute nonlymphocytic	0	0.05	0.0	0	0.06	0.0	0	0.03	0.0	0	0.04	0.0	0	0.19	0.0

[a] ICD-O codes = 155–156.

[b] $P < .05$.

PANCREAS
BOTH SEXES

TABLE 7A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the pancreas, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,655	2,317	4,972
No. who developed a second primary cancer	29	11	40
Average age at diagnosis of first cancer, yr	64	67	65
Average yr of diagnosis of first cancer	1967	1967	1967
Person-yr of follow-up	1,547	1,536	3,083
Average follow-up, yr	0.6	0.7	0.6
Percent given radiotherapy for first cancer	11.6	9.2	10.5

[a] ICD-O code = 157.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 7B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the pancreas in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	33	82.5
Only the first cancer	3	7.5
Only the second cancer	4	10.0
Neither first nor second cancer	0	0.0
Total second primary cancers	40	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

PANCREAS
BOTH SEXES

TABLE 7C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pancreas among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,972			925			91			33			4,972		
Person-yr in interval	1,670			953			275			185			3,083		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**22**	**21.17**	**1.0**	**13**	**12.61**	**1.0**	**2**	**3.74**	**0.5**	**3**	**2.46**	**1.2**	**40**	**39.95**	**1.0**
All excluding site of initial cancer	**22**	**20.47**	**1.1**	**13**	**12.19**	**1.1**	**2**	**3.62**	**0.6**	**3**	**2.38**	**1.3**	**40**	**38.64**	**1.0**
Buccal cavity, pharynx	**0**	**0.77**	**0.0**	**1**	**0.44**	**2.3**	**0**	**0.12**	**0.0**	**0**	**0.07**	**0.0**	**1**	**1.40**	**0.7**
Lip	0	0.12	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.21	0.0
Tongue	0	0.16	0.0	0	0.09	0.0	0	0.02	0.0	0	0.01	0.0	0	0.28	0.0
Salivary gland	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Gum, other mouth	0	0.23	0.0	0	0.13	0.0	0	0.04	0.0	0	0.02	0.0	0	0.42	0.0
Pharynx	0	0.19	0.0	1	0.11	9.3	0	0.03	0.0	0	0.02	0.0	1	0.34	2.9
Digestive system	**4**	**6.77**	**0.6**	**1**	**3.99**	**0.3**	**0**	**1.15**	**0.0**	**2**	**0.76**	**2.6**	**7**	**12.66**	**0.6**
Esophagus	0	0.33	0.0	0	0.18	0.0	0	0.05	0.0	0	0.03	0.0	0	0.59	0.0
Stomach	0	1.06	0.0	0	0.61	0.0	0	0.15	0.0	0	0.09	0.0	0	1.91	0.0
Colon	3	2.83	1.1	1	1.70	0.6	0	0.52	0.0	1	0.35	2.8	5	5.39	0.9
Rectum	1	1.35	0.7	0	0.80	0.0	0	0.23	0.0	0	0.15	0.0	1	2.53	0.4
Liver, biliary	0	0.39	0.0	0	0.22	0.0	0	0.06	0.0	1	0.05	21.9	1	0.72	1.4
Pancreas	0	0.70	0.0	0	0.42	0.0	0	0.12	0.0	0	0.08	0.0	0	1.31	0.0
Respiratory system	**2**	**3.16**	**0.6**	**1**	**1.87**	**0.5**	**0**	**0.57**	**0.0**	**1**	**0.33**	**3.1**	**4**	**5.91**	**0.7**
Nasal cavities, sinuses	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.08	0.0
Larynx	0	0.32	0.0	0	0.18	0.0	0	0.05	0.0	0	0.03	0.0	0	0.57	0.0
Trachea, bronchus, lung	1	2.77	0.4	1	1.65	0.6	0	0.50	0.0	1	0.29	3.4	3	5.21	0.6
Female breast	1	2.11	0.5	3	1.21	2.5	0	0.37	0.0	0	0.32	0.0	4	4.00	1.0
Female genital tract	**0**	**1.28**	**0.0**	**2**	**0.73**	**2.8**	**1**	**0.21**	**4.7**	**0**	**0.19**	**0.0**	**3**	**2.41**	**1.2**
Cervix uteri	0	0.22	0.0	0	0.12	0.0	0	0.04	0.0	0	0.03	0.0	0	0.41	0.0
Corpus uteri	0	0.54	0.0	0	0.31	0.0	1	0.09	10.6	0	0.08	0.0	1	1.04	1.0
Uterus, NOS	0	0.08	0.0	1	0.04	23.9	0	0.01	0.0	0	0.01	0.0	1	0.14	7.0
Ovary, fallopian tubes	0	0.35	0.0	1	0.20	5.0	0	0.06	0.0	0	0.05	0.0	1	0.67	1.5
Prostate gland	11	2.31	4.8[b]	4	1.52	2.6	1	0.47	2.1	0	0.24	0.0	16	4.54	3.5[b]
Testis	1	0.02	53.3	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	1	0.03	30.0
Kidney, renal pelvis, ureter	1	0.45	2.2	0	0.27	0.0	0	0.08	0.0	0	0.05	0.0	1	0.85	1.2
Bladder, other urinary	0	1.17	0.0	0	0.72	0.0	0	0.22	0.0	0	0.13	0.0	0	2.25	0.0
Melanoma of the skin	0	0.23	0.0	0	0.13	0.0	0	0.04	0.0	0	0.03	0.0	0	0.44	0.0
Eye	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.06	0.0
Brain, central nervous system	0	0.21	0.0	0	0.12	0.0	0	0.04	0.0	0	0.03	0.0	0	0.39	0.0
Thyroid gland	1	0.09	11.5	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	1	0.16	6.2
Bone	0	0.03	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.05	0.0
Connective tissue	1	0.10	10.5	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	1	0.18	5.6
Lymphatic, hematopoietic system	**0**	**1.40**	**0.0**	**1**	**0.84**	**1.2**	**0**	**0.26**	**0.0**	**0**	**0.17**	**0.0**	**1**	**2.67**	**0.4**
Non-Hodgkin's lymphoma	0	0.48	0.0	1	0.29	3.5	0	0.09	0.0	0	0.06	0.0	1	0.92	1.1
Hodgkin's disease	0	0.09	0.0	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	0	0.17	0.0
Multiple myeloma	0	0.23	0.0	0	0.14	0.0	0	0.05	0.0	0	0.03	0.0	0	0.45	0.0
Leukemias	0	0.59	0.0	0	0.36	0.0	0	0.11	0.0	0	0.07	0.0	0	1.13	0.0
Chronic lymphocytic	0	0.19	0.0	0	0.11	0.0	0	0.04	0.0	0	0.02	0.0	0	0.36	0.0
Acute nonlymphocytic	0	0.18	0.0	0	0.11	0.0	0	0.04	0.0	0	0.03	0.0	0	0.36	0.0

[a] ICD-O code = 157.

[b] $P < .05$.

PANCREAS
MALES

TABLE 7D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pancreas among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,655			491			46			18			2,655		
Person-yr in interval	871			484			131			62			1,547		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**21**	**12.65**	**1.7^b**	**6**	**7.77**	**0.8**	**1**	**2.28**	**0.4**	**1**	**1.17**	**0.9**	**29**	**23.85**	**1.2**
All excluding site of initial cancer	**21**	**12.24**	**1.7^b**	**6**	**7.52**	**0.8**	**1**	**2.21**	**0.5**	**1**	**1.14**	**0.9**	**29**	**23.08**	**1.3**
Buccal cavity, pharynx	**0**	**0.63**	**0.0**	**0**	**0.36**	**0.0**	**0**	**0.09**	**0.0**	**0**	**0.05**	**0.0**	**0**	**1.12**	**0.0**
Lip	0	0.11	0.0	0	0.06	0.0	0	0.01	0.0	0	0.01	0.0	0	0.19	0.0
Tongue	0	0.12	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.22	0.0
Salivary gland	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.06	0.0
Gum, other mouth	0	0.18	0.0	0	0.10	0.0	0	0.03	0.0	0	0.01	0.0	0	0.32	0.0
Pharynx	0	0.16	0.0	0	0.09	0.0	0	0.02	0.0	0	0.01	0.0	0	0.28	0.0
Digestive system	**4**	**4.01**	**1.0**	**0**	**2.45**	**0.0**	**0**	**0.68**	**0.0**	**0**	**0.35**	**0.0**	**4**	**7.48**	**0.5**
Esophagus	0	0.27	0.0	0	0.15	0.0	0	0.04	0.0	0	0.02	0.0	0	0.47	0.0
Stomach	0	0.71	0.0	0	0.42	0.0	0	0.10	0.0	0	0.05	0.0	0	1.29	0.0
Colon	3	1.51	2.0	0	0.95	0.0	0	0.29	0.0	0	0.15	0.0	3	2.89	1.0
Rectum	1	0.84	1.2	0	0.51	0.0	0	0.14	0.0	0	0.07	0.0	1	1.56	0.6
Liver, biliary	0	0.21	0.0	0	0.12	0.0	0	0.03	0.0	0	0.02	0.0	0	0.38	0.0
Pancreas	0	0.41	0.0	0	0.25	0.0	0	0.07	0.0	0	0.03	0.0	0	0.77	0.0
Respiratory system	**2**	**2.62**	**0.8**	**1**	**1.55**	**0.6**	**0**	**0.47**	**0.0**	**1**	**0.24**	**4.1**	**4**	**4.88**	**0.8**
Nasal cavities, sinuses	0	0.03	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.05	0.0
Larynx	0	0.29	0.0	0	0.16	0.0	0	0.04	0.0	0	0.02	0.0	0	0.52	0.0
Trachea, bronchus, lung	1	2.28	0.4	1	1.36	0.7	0	0.42	0.0	1	0.22	4.7	3	4.26	0.7
Prostate gland	11	2.31	4.8^b	4	1.52	2.6	1	0.47	2.1	0	0.24	0.0	16	4.54	3.5^b
Testis	1	0.02	53.3	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	1	0.03	30.0
Kidney, renal pelvis, ureter	1	0.32	3.2	0	0.19	0.0	0	0.06	0.0	0	0.03	0.0	1	0.59	1.7
Bladder, other urinary	0	0.92	0.0	0	0.57	0.0	0	0.18	0.0	0	0.09	0.0	0	1.76	0.0
Melanoma of the skin	0	0.14	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.27	0.0
Eye	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Brain, central nervous system	0	0.13	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.24	0.0
Thyroid gland	1	0.03	30.3	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	1	0.06	16.7
Bone	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Connective tissue	1	0.06	16.4	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	1	0.11	8.8
Lymphatic, hematopoietic system	**0**	**0.83**	**0.0**	**1**	**0.51**	**2.0**	**0**	**0.15**	**0.0**	**0**	**0.08**	**0.0**	**1**	**1.56**	**0.6**
Non-Hodgkin's lymphoma	0	0.27	0.0	1	0.16	6.2	0	0.05	0.0	0	0.03	0.0	1	0.51	2.0
Hodgkin's disease	0	0.06	0.0	0	0.03	0.0	0	0.01	0.0	0	0.00	0.0	0	0.10	0.0
Multiple myeloma	0	0.13	0.0	0	0.08	0.0	0	0.03	0.0	0	0.01	0.0	0	0.25	0.0
Leukemias	0	0.37	0.0	0	0.23	0.0	0	0.07	0.0	0	0.04	0.0	0	0.71	0.0
Chronic lymphocytic	0	0.12	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.23	0.0
Acute nonlymphocytic	0	0.11	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.22	0.0

[a] ICD-O code = 157.

[b] $P < .05$.

PANCREAS FEMALES

TABLE 7E. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pancreas among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,317			434			45			15			2,317		
Person-yr in interval	799			470			144			123			1,536		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1**	**8.52**	**0.1**[b]	**7**	**4.84**	**1.4**	**1**	**1.46**	**0.7**	**2**	**1.29**	**1.5**	**11**	**16.11**	**0.7**
All excluding site of initial cancer	**1**	**8.23**	**0.1**[b]	**7**	**4.68**	**1.5**	**1**	**1.41**	**0.7**	**2**	**1.25**	**1.6**	**11**	**15.57**	**0.7**
Buccal cavity, pharynx	**0**	**0.15**	**0.0**	**1**	**0.08**	**12.0**	**0**	**0.03**	**0.0**	**0**	**0.02**	**0.0**	**1**	**0.28**	**3.6**
Lip	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Tongue	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.06	0.0
Salivary gland	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Gum, other mouth	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Pharynx	0	0.03	0.0	1	0.02	54.6	0	0.01	0.0	0	0.00	0.0	1	0.06	16.6
Digestive system	**0**	**2.77**	**0.0**	**1**	**1.54**	**0.6**	**0**	**0.47**	**0.0**	**2**	**0.41**	**4.8**	**3**	**5.19**	**0.6**
Esophagus	0	0.06	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.11	0.0
Stomach	0	0.35	0.0	0	0.18	0.0	0	0.05	0.0	0	0.04	0.0	0	0.62	0.0
Colon	0	1.32	0.0	1	0.74	1.3	0	0.23	0.0	1	0.20	4.9	2	2.50	0.8
Rectum	0	0.51	0.0	0	0.29	0.0	0	0.09	0.0	0	0.08	0.0	0	0.97	0.0
Liver, biliary	0	0.19	0.0	0	0.10	0.0	0	0.03	0.0	1	0.03	38.4	1	0.34	2.9
Pancreas	0	0.29	0.0	0	0.16	0.0	0	0.05	0.0	0	0.04	0.0	0	0.54	0.0
Respiratory system	**0**	**0.54**	**0.0**	**0**	**0.32**	**0.0**	**0**	**0.10**	**0.0**	**0**	**0.08**	**0.0**	**0**	**1.04**	**0.0**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Larynx	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.06	0.0
Trachea, bronchus, lung	0	0.49	0.0	0	0.29	0.0	0	0.09	0.0	0	0.08	0.0	0	0.94	0.0
Female breast	1	2.11	0.5	3	1.21	2.5	0	0.37	0.0	0	0.32	0.0	4	4.00	1.0
Female genital tract	**0**	**1.28**	**0.0**	**2**	**0.73**	**2.8**	**1**	**0.21**	**4.7**	**0**	**0.19**	**0.0**	**3**	**2.41**	**1.2**
Cervix uteri	0	0.22	0.0	0	0.12	0.0	0	0.04	0.0	0	0.03	0.0	0	0.41	0.0
Corpus uteri	0	0.54	0.0	0	0.31	0.0	1	0.09	10.6	0	0.08	0.0	1	1.04	1.0
Uterus, NOS	0	0.08	0.0	1	0.04	23.9	0	0.01	0.0	0	0.01	0.0	1	0.14	7.0
Ovary, fallopian tubes	0	0.35	0.0	1	0.20	5.0	0	0.06	0.0	0	0.05	0.0	1	0.67	1.5
Kidney, renal pelvis, ureter	0	0.14	0.0	0	0.08	0.0	0	0.02	0.0	0	0.02	0.0	0	0.26	0.0
Bladder, other urinary	0	0.26	0.0	0	0.15	0.0	0	0.05	0.0	0	0.04	0.0	0	0.49	0.0
Melanoma of the skin	0	0.09	0.0	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.17	0.0
Eye	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Brain, central nervous system	0	0.08	0.0	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	0	0.15	0.0
Thyroid gland	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Connective tissue	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Lymphatic, hematopoietic system	**0**	**0.57**	**0.0**	**0**	**0.33**	**0.0**	**0**	**0.11**	**0.0**	**0**	**0.09**	**0.0**	**0**	**1.10**	**0.0**
Non-Hodgkin's lymphoma	0	0.21	0.0	0	0.12	0.0	0	0.04	0.0	0	0.03	0.0	0	0.41	0.0
Hodgkin's disease	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Multiple myeloma	0	0.10	0.0	0	0.06	0.0	0	0.02	0.0	0	0.02	0.0	0	0.21	0.0
Leukemias	0	0.22	0.0	0	0.13	0.0	0	0.04	0.0	0	0.04	0.0	0	0.42	0.0
Chronic lymphocytic	0	0.06	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.13	0.0
Acute nonlymphocytic	0	0.07	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.14	0.0

[a] ICD-O code = 157.

[b] $P < .05$.

Second Cancer Following Cancer of the Respiratory System in Connecticut, 1935–1982 [1]

John D. Boice, Jr. [2] *and* Joseph F. Fraumeni, Jr. [3]

ABSTRACT—The risk of a person developing a second primary cancer was evaluated in approximately 30,000 persons who developed cancer of the respiratory system in Connecticut between 1935 and 1982. A significant 44% excess of all second cancers was observed following cancer of the lung (614 observed vs. 426 expected). The excess of second tumors was 72% following cancer of the larynx (541 vs. 314) and 34% following cancer of the nasal cavities and sinuses (43 vs. 32). For cancers of the lung and larynx, second cancers arose mainly along the respiratory tract or other sites associated with cigarette smoking (oral cavity, bladder, kidney). A threefold excess of esophageal cancer followed cancer of the larynx, which was indicative of risk factors in common (alcohol and tobacco) and possibly an effect of radiotherapy. Radiotherapy may have contributed also to the increased risk of second lung and breast cancers. A slight excess risk of leukemia after lung cancer points to a possible effect of chemotherapy given for certain histologic types. An unexpected finding was a significant 50% increased risk of colon cancer following cancer of the larynx. Significant excesses of prostate cancer are probably artifacts associated with increased medical surveillance and higher autopsy rates among cancer patients than in the general population. No deficits of any second cancers were observed. The risk of a second cancer developing did not appear to vary by sex or time since initial diagnosis, except that the risks following cancer of the nasal cavities and sinuses returned to normal levels among long-term survivors. Among persons observed for 10 or more years after their initial diagnosis of cancers of the lung or larynx, the risk of developing a second cancer remained high, i.e., on the order of 50% above expectation. Further analytic studies should clarify the role of smoking, alcohol, other life-style and host factors, and various forms of therapy on the risk of second cancers following cancer of the respiratory system.—Natl Cancer Inst Monogr 68: 83–98, 1985.

TRACHEA, BRONCHUS, LUNG (ICD-O, 162)

Primary lung cancer represents about 16% of all cancers occurring in the United States (22% in males and 10% in females). However, because case fatality rates are high, lung cancer accounts for 27% of all cancer deaths or 35% in males and 18% in females (*1*). The predominant risk factor is cigarette smoking, with industrial exposures contributing to some extent (*2*). The 5-year survival rate has increased slightly over the years, from 7 to 10% for men and 11 to 15% for women over the periods from 1960–63 to 1973–79 (*3, 4*). Among all patients with localized disease, the 5-year survival rates rose from 21 to 33%. However at the time of diagnosis, 70% of the patients with lung cancer present with disease that has already spread to regional nodes or distant sites, and most patients die within the first year of diagnosis (*5*). Among 64,000 lung cancer patients reported to the Surveillance, Epidemiology, and End Results Program between 1973 and 1980, initial treatment was surgery only in 18%, radiotherapy without chemotherapy in 35%, chemotherapy with or without radiotherapy in 21%, and other treatments or none in 27% (*6*).

Previous studies of second tumors among patients with lung cancer have indicated excess cancers of the oral cavity, larynx, bladder, cervix, and other smoking-related sites (*7–11*). In an earlier survey in Connecticut, patients with lung cancer showed a pattern of increased risks mainly involving prostate and kidney cancers (*12*).

Results

Between 1935 and 1982 in Connecticut, 24,423 persons developed lung cancer. The average age at diagnosis was 62 years, and the average follow-up was only 1.3 years. The average year of diagnosis was 1970. Males were three times as likely to develop lung cancer as were females. Over 50% of the patients initially received radiotherapy, 22% were treated only with surgical resection, and 21% received other or no therapy. Overall, 614 (or 2.5%) of the lung cancer patients developed a second cancer, compared with 426 expected on the basis of rates in the general population (RR = 1.44; 95% CI = 1.33–1.56).

Cancers of the lung (RR = 1.5; n = 110) and prostate (RR = 2.0; n = 121) were the most frequent second primary neoplasms. Significant excesses were also found for cancers of the tongue, salivary gland, pharynx, and kidney. Nonsignificant excesses were observed for cancers of the stomach, rectum, pancreas, breast, and ANLL. The risk of developing a second cancer was slightly higher in females (RR = 1.6) than in males (1.4), with excess cancers of the bladder and pancreas and ANLL seen mainly in males. No sites occurred significantly below expectation.

Excess second cancers persisted among the 577 persons surviving 10 or more years after the initial diagnosis of

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ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia;

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Radiation Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3A22, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* John D. Boice, Jr., Sc.D.

[3] Epidemiology and Biostatistics Program, Division of Cancer Etiology.

lung cancer (RR = 1.5; 95% CI = 1.2–1.9). This group experienced significantly high risks of second lung cancer and cancer of the bladder. Overall, the pattern of second cancer occurrence did not vary over time since first diagnosis, and significant risks were observed in all intervals. However, the risk of developing a second lung cancer increased over time ($P < .001$ for trend), as did the risk for bladder cancer ($P = .02$). Although based on only 4 cases, the risk of cervical cancer also appeared to increase over time since diagnosis. The risk of prostate and kidney cancers decreased with time.

Discussion

Persons with lung cancer showed a significant 44% increased risk of developing a second primary cancer throughout subsequent years of survival. Most of the excess cancers were tobacco related, notably cancers of the oral cavity, bladder, kidney, larynx, and second lung (*13*). The risk of bladder cancer and second lung cancer increased significantly over time. The lung was the site for 1 of every 6 second cancers, but it is difficult from the available data for one to distinguish between multifocal neoplasms or misdiagnosed metastases (*14*). The slight risk of ANLL might be associated with chemotherapy; several clinical reports have linked ANLL with alkylating agents used to treat small cell carcinoma of the lung (*15, 16*). The excess of prostate cancer is probably an artifact due to medical surveillance bias, particularly because the risk decreased significantly with time since diagnosis. In addition, because autopsy rates are higher in patients with cancer than in the general population, physicians have more opportunity to detect and report occult primary cancers of the prostate (*12*). Fifty-three of the 121 prostate cancers (or 44%) were detected at autopsy. The small excess of cervical cancer following lung cancer is noteworthy in view of the large increase of lung cancer reported after cervical cancer (*17*). This is consistent with recent evidence that smoking may increase the risk of cervical cancer (*18*), although life-style and socioeconomic variables correlated with smoking habits must be considered as well. The elevated risk of kidney cancer may also be associated with smoking habits that increase the risk for both renal cell carcinoma (*19*) and renal pelvis cancer (*20*). The slight risk of breast cancer that appeared to increase over time is interesting, particularly because an excess of lung cancer following breast cancer was also seen in Connecticut (*21*). Radiotherapy might contribute to these risks, inasmuch as breast and lung tissue are both sensitive to the carcinogenic effects of ionizing radiation (*22*). The excess of salivary gland cancer is interesting because this tissue is also radiosensitive and because lung cancer occurred excessively in patients with salivary gland cancer in Connecticut (*23*) and in a British series (*24*).

LARYNX (ICD-O, 161)

Cancer of the larynx represents about 1.3% of all cancers occurring in the United States, with higher rates in males than females (*1*). The primary risk factors are tobacco smoking and alcohol consumption, with some occupational exposures also implicated (*25*). Five-year relative survival rates are on the order of 65% for both males and females (*3, 4*). The earlier study of laryngeal cancer in Connecticut revealed increased rates for cancers of the tongue, lung, and prostate (*12*), whereas other surveys have emphasized excess risks of various cancers linked to cigarette smoking and alcohol intake (*7–11, 26–28*). The risk of a second primary cancer developing has been linked mainly to smoking and drinking habits before the onset of the initial cancer, although continued smoking and drinking may augment the risk (*10, 11*).

Results

Among 4,139 persons with cancer of the larynx, 541 (or 13.1%) developed a second primary cancer (RR = 1.72; 95% CI = 1.58–1.87). The average age at diagnosis of laryngeal cancer was 61 years, and the average follow-up was 5.3 years. The average year of diagnosis was 1966. Males were seven times more likely to develop laryngeal cancer than were females. Almost 60% of the population received radiation as initial treatment.

Lung cancer accounted for 33% of all second cancers (RR = 3.2; 95% CI = 2.8–3.7). Significant excesses were also found for cancers of the tongue (RR = 3.7; $n = 11$), gum and mouth (RR = 3.1; $n = 13$), pharynx (RR = 3.2; $n = 12$), esophagus (RR = 3.1; $n = 19$), and colon (RR = 1.5; $n = 57$). Cancer of the rectum was not increased (RR = 0.9; $n = 19$). No sites occurred significantly below expectation based on general population rates. The risk of a second cancer developing did not vary appreciably by sex or time since initial diagnosis of laryngeal cancer. Among 782 persons who survived 10 or more years beyond their initial diagnosis, 141 (or 18%) developed a second cancer (RR = 1.6; 95% CI = 1.4–1.9).

Discussion

This survey of patients with laryngeal cancer revealed a significant 72% excess risk of patients developing a second primary cancer. Most second cancers could be attributed to underlying smoking habits (lung cancer) or to the interaction of smoking and drinking, i.e., cancers of oral cavity, pharynx, and esophagus (*11*). This striking pattern of multiple primary neoplasms illustrates the role of shared risk factors and possibly a regional tissue susceptibility that could interact with these factors (*8*). Thus it is important that patients with laryngeal cancer avoid or limit exposure to tobacco and alcohol and undergo medical surveillance aimed at early detection of second cancers of the upper digestive tract and respiratory system (*26–29*). Case reports suggest that radiotherapy for laryngeal and other cancers can also influence the development of adjacent cancers, especially of the esophagus (*27, 30*), but the risk of this particular tumor did not increase over time. It is noteworthy that cancer of the thyroid, an especially radiosensitive site, was not increased above expectation. The risk of prostate cancer was elevated, which is consistent with the increased diagnostic surveillance of cancer patients. The significant excess of colon cancer following laryngeal cancer should be noted, particularly because colon cancer also occurred excessively among patients with oral cancer in Connecticut (*23*). Although further investigation is needed for clarification of the association between these tumors, some recent studies have suggested that alcohol intake, notably beer drinking, increases the risk of colorectal cancer (*31*) as well as laryngeal and oral cancer.

NASAL CAVITIES AND PARANASAL SINUSES (ICD-O, 160)

Cancers of the nasal cavities and paranasal sinuses account for only about 0.2% of all cancers in the United States. The 5-year relative survival rate is approximately 50% for men and women (*3*). Several occupational hazards have been implicated, including exposures to nickel, wood dust, chromates, textiles, radium, leather dust, and petroleum products (*32*). Recently, cigarette smoking was linked to cancer of the nasal cavities (*33*). Few studies of multiple primary cancers have been conducted among patients with nasal cancer, although a small elevation of breast cancer was reported in the earlier survey from Connecticut (*12*).

Results

Between 1935 and 1982, a total of 620 persons developed nasal cancer in Connecticut. The average age at diagnosis was 60 years, and the average follow-up was 4.4 years. The average year of diagnosis was 1963. Males were 1.4 times more likely to develop this cancer than females. More than 65% of the patients were treated initially with radiation. Overall, 43 (or 6.9%) of all patients developed a second cancer compared with 32.2 expected (RR = 1.34; 95% CI = 0.97–1.80). Risks were elevated for cancers of the lung (RR = 2.1; $n = 9$), female breast (2.3; $n = 6$), and non-Hodgkin's lymphoma (4.2; $n = 3$), although the numbers involved were small and the differences were not significant. The risk of developing a second cancer for all sites combined decreased significantly with time since initial diagnosis ($P = .004$) and returned to normal levels among long-term survivors. Among the 90 individuals who survived 10 or more years after diagnosis of nasal cancer, only 9 second cancers occurred versus 10.3 expected.

Discussion

In this series of patients with nasal cancer, the risk of second cancers was increased (34%), most notably for cancers of the lung and breast and non-Hodgkin's lymphoma. The results for individual sites were based on small numbers and were not statistically significant. However, the risk for subsequent cancers returned to normal levels among long-term survivors in contrast to the persistent elevation of second tumors following cancers of the lung and larynx. The findings are consistent with other surveys (*7*) and suggest that the major risk factors or susceptibility mechanisms underlying cancers of the upper digestive and respiratory tracts do not apply to cancers of the nasal passages.

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NASAL CAVITIES
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the nasal cavities or sinuses, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	361	259	620
No. who developed a second primary cancer	22	21	43
Average age at diagnosis of first cancer, yr	61	59	60
Average yr of diagnosis of first cancer	1962	1963	1963
Person-yr of follow-up	1,608	1,142	2,750
Average follow-up, yr	4.5	4.4	4.4
Percent given radiotherapy for first cancer	65.1	66.4	65.6

[a] ICD-O code = 160.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the nasal cavities or sinuses in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	35	81.4
Only the first cancer	8	18.6
Only the second cancer	0	0.0
Neither first nor second cancer	0	0.0
Total second primary cancers	43	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

NASAL CAVITIES
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the nasal cavities or sinuses among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	620			413			175			90			620		
Person-yr in interval	427			1,011			631			680			2,750		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**4.46**	**0.4**	**21**	**10.52**	**2.0**[b]	**11**	**6.97**	**1.6**	**9**	**10.25**	**0.9**	**43**	**32.18**	**1.3**
All excluding site of initial cancer	**2**	**4.45**	**0.4**	**21**	**10.50**	**2.0**[b]	**11**	**6.96**	**1.6**	**9**	**10.23**	**0.9**	**43**	**32.11**	**1.3**
Buccal cavity, pharynx	**0**	**0.18**	**0.0**	**2**	**0.42**	**4.8**	**0**	**0.28**	**0.0**	**0**	**0.39**	**0.0**	**2**	**1.27**	**1.6**
Lip	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.07	0.0	0	0.22	0.0
Tongue	0	0.04	0.0	1	0.08	12.1	0	0.05	0.0	0	0.08	0.0	1	0.25	4.0
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Gum, other mouth	0	0.05	0.0	1	0.12	8.4	0	0.08	0.0	0	0.11	0.0	1	0.36	2.8
Pharynx	0	0.04	0.0	0	0.10	0.0	0	0.07	0.0	0	0.09	0.0	0	0.31	0.0
Digestive system	**0**	**1.45**	**0.0**	**3**	**3.35**	**0.9**	**2**	**2.20**	**0.9**	**2**	**3.24**	**0.6**	**7**	**10.22**	**0.7**
Esophagus	0	0.08	0.0	0	0.17	0.0	0	0.11	0.0	0	0.17	0.0	0	0.53	0.0
Stomach	0	0.26	0.0	1	0.57	1.8	0	0.36	0.0	0	0.51	0.0	1	1.70	0.6
Colon	0	0.57	0.0	1	1.35	0.7	1	0.89	1.1	0	1.35	0.0	2	4.16	0.5
Rectum	0	0.29	0.0	0	0.67	0.0	0	0.44	0.0	2	0.64	3.1	2	2.04	1.0
Liver, biliary	0	0.08	0.0	0	0.19	0.0	0	0.12	0.0	0	0.18	0.0	0	0.58	0.0
Pancreas	0	0.14	0.0	0	0.34	0.0	0	0.23	0.0	0	0.33	0.0	0	1.04	0.0
Respiratory system	**0**	**0.65**	**0.0**	**3**	**1.56**	**1.9**	**4**	**1.08**	**3.7**	**3**	**1.69**	**1.8**	**10**	**4.98**	**2.0**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.07	0.0
Larynx	0	0.07	0.0	0	0.17	0.0	1	0.11	8.8	0	0.16	0.0	1	0.52	1.9
Trachea, bronchus, lung	0	0.56	0.0	3	1.35	2.2	3	0.94	3.2	3	1.49	2.0	9	4.35	2.1
Female breast	1	0.39	2.6	3	1.02	2.9	2	0.66	3.0	0	0.59	0.0	6	2.66	2.3
Female genital tract	**0**	**0.25**	**0.0**	**1**	**0.62**	**1.6**	**0**	**0.40**	**0.0**	**1**	**0.34**	**2.9**	**2**	**1.61**	**1.2**
Cervix uteri	0	0.05	0.0	0	0.12	0.0	0	0.07	0.0	0	0.06	0.0	0	0.30	0.0
Corpus uteri	0	0.10	0.0	0	0.25	0.0	0	0.17	0.0	1	0.15	6.9	1	0.66	1.5
Uterus, NOS	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.11	0.0
Ovary, fallopian tubes	0	0.07	0.0	1	0.17	5.8	0	0.11	0.0	0	0.09	0.0	1	0.44	2.3
Prostate gland	0	0.54	0.0	1	1.18	0.8	1	0.78	1.3	2	1.60	1.2	4	4.10	1.0
Testis	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Kidney, renal pelvis, ureter	0	0.10	0.0	1	0.22	4.5	0	0.15	0.0	0	0.22	0.0	1	0.69	1.4
Bladder, other urinary	0	0.25	0.0	1	0.58	1.7	0	0.39	0.0	0	0.67	0.0	1	1.89	0.5
Melanoma of the skin	0	0.05	0.0	0	0.12	0.0	0	0.07	0.0	0	0.10	0.0	0	0.34	0.0
Eye	0	0.01	0.0	1	0.02	58.5	0	0.01	0.0	0	0.01	0.0	1	0.05	20.4
Brain, central nervous system	0	0.04	0.0	1	0.11	9.1	0	0.07	0.0	0	0.09	0.0	1	0.32	3.2
Thyroid gland	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.05	0.0	0	0.15	0.0
Lymphatic, hematopoietic system	**1**	**0.28**	**3.5**	**3**	**0.68**	**4.4**	**1**	**0.46**	**2.2**	**0**	**0.69**	**0.0**	**5**	**2.11**	**2.4**
Non-Hodgkin's lymphoma	0	0.10	0.0	2	0.24	8.5	1	0.16	6.4	0	0.22	0.0	3	0.71	4.2
Hodgkin's disease	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.04	0.0	0	0.15	0.0
Multiple myeloma	0	0.04	0.0	1	0.11	9.3	0	0.07	0.0	0	0.11	0.0	1	0.33	3.0
Leukemias	1	0.12	8.2	0	0.29	0.0	0	0.19	0.0	0	0.31	0.0	1	0.92	1.1
Chronic lymphocytic	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.10	0.0	0	0.29	0.0
Acute nonlymphocytic	1	0.03	28.6	0	0.08	0.0	0	0.06	0.0	0	0.10	0.0	1	0.28	3.6

[a] ICD-O code = 160.

[b] $P < .05$.

NASAL CAVITIES
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the nasal cavities or sinuses among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval		361			240			95			52			361	
Person-yr in interval		246			564			348			449			1,608	
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1**	**2.96**	**0.3**	**10**	**6.59**	**1.5**	**5**	**4.42**	**1.1**	**6**	**7.86**	**0.8**	**22**	**21.80**	**1.0**
All excluding site of initial cancer	**1**	**2.95**	**0.3**	**10**	**6.58**	**1.5**	**5**	**4.41**	**1.1**	**6**	**7.84**	**0.8**	**22**	**21.75**	**1.0**
Buccal cavity, pharynx	**0**	**0.16**	**0.0**	**1**	**0.35**	**2.9**	**0**	**0.23**	**0.0**	**0**	**0.35**	**0.0**	**1**	**1.08**	**0.9**
Lip	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.06	0.0	0	0.20	0.0
Tongue	0	0.03	0.0	1	0.07	14.6	0	0.04	0.0	0	0.07	0.0	1	0.21	4.7
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Gum, other mouth	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.10	0.0	0	0.29	0.0
Pharynx	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.09	0.0	0	0.27	0.0
Digestive system	**0**	**0.98**	**0.0**	**2**	**2.12**	**0.9**	**1**	**1.41**	**0.7**	**1**	**2.46**	**0.4**	**4**	**6.96**	**0.6**
Esophagus	0	0.07	0.0	0	0.15	0.0	0	0.10	0.0	0	0.15	0.0	0	0.46	0.0
Stomach	0	0.20	0.0	0	0.40	0.0	0	0.26	0.0	0	0.41	0.0	0	1.27	0.0
Colon	0	0.35	0.0	1	0.77	1.3	0	0.52	0.0	0	0.98	0.0	1	2.62	0.4
Rectum	0	0.20	0.0	0	0.44	0.0	0	0.29	0.0	1	0.50	2.0	1	1.43	0.7
Liver, biliary	0	0.05	0.0	0	0.11	0.0	0	0.07	0.0	0	0.13	0.0	0	0.36	0.0
Pancreas	0	0.10	0.0	0	0.21	0.0	0	0.15	0.0	0	0.25	0.0	0	0.71	0.0
Respiratory system	**0**	**0.56**	**0.0**	**1**	**1.31**	**0.8**	**3**	**0.91**	**3.3**	**3**	**1.53**	**2.0**	**7**	**4.32**	**1.6**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Larynx	0	0.07	0.0	0	0.15	0.0	1	0.10	9.7	0	0.15	0.0	1	0.48	2.1
Trachea, bronchus, lung	0	0.48	0.0	1	1.13	0.9	2	0.79	2.5	3	1.35	2.2	6	3.76	1.6
Prostate gland	0	0.54	0.0	1	1.18	0.8	1	0.78	1.3	2	1.60	1.2	4	4.10	1.0
Testis	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Kidney, renal pelvis, ureter	0	0.07	0.0	1	0.16	6.1	0	0.11	0.0	0	0.19	0.0	1	0.53	1.9
Bladder, other urinary	0	0.21	0.0	1	0.47	2.1	0	0.32	0.0	0	0.59	0.0	1	1.59	0.6
Melanoma of the skin	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.08	0.0	0	0.22	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Brain, central nervous system	0	0.03	0.0	1	0.07	14.1	0	0.05	0.0	0	0.07	0.0	1	0.22	4.6
Thyroid gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.04	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**1**	**0.19**	**5.3**	**2**	**0.43**	**4.6**	**0**	**0.29**	**0.0**	**0**	**0.53**	**0.0**	**3**	**1.44**	**2.1**
Non-Hodgkin's lymphoma	0	0.06	0.0	1	0.14	7.1	0	0.10	0.0	0	0.16	0.0	1	0.46	2.2
Hodgkin's disease	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.10	0.0
Multiple myeloma	0	0.03	0.0	1	0.06	15.6	0	0.04	0.0	0	0.08	0.0	1	0.22	4.6
Leukemias	1	0.09	11.5	0	0.19	0.0	0	0.13	0.0	0	0.25	0.0	1	0.66	1.5
Chronic lymphocytic	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.08	0.0	0	0.22	0.0
Acute nonlymphocytic	1	0.02	42.5	0	0.05	0.0	0	0.04	0.0	0	0.08	0.0	1	0.19	5.2

[a] ICD-O code = 160.

[b] $P < .05$.

NASAL CAVITIES
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the nasal cavities or sinuses among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	259			173			80			38			259		
Person-yr in interval	181			447			283			231			1,142		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1**	**1.51**	**0.7**	**11**	**3.94**	**2.8**[b]	**6**	**2.55**	**2.4**	**3**	**2.39**	**1.3**	**21**	**10.38**	**2.0**[b]
All excluding site of initial cancer	**1**	**1.51**	**0.7**	**11**	**3.93**	**2.8**[b]	**6**	**2.55**	**2.4**	**3**	**2.39**	**1.3**	**21**	**10.36**	**2.0**[b]
Buccal cavity, pharynx	**0**	**0.03**	**0.0**	**1**	**0.07**	**14.3**	**0**	**0.05**	**0.0**	**0**	**0.04**	**0.0**	**1**	**0.18**	**5.4**
Lip	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Tongue	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Salivary gland	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.02	0.0
Gum, other mouth	0	0.01	0.0	1	0.02	42.2	0	0.02	0.0	0	0.02	0.0	1	0.06	15.6
Pharynx	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Digestive system	**0**	**0.47**	**0.0**	**1**	**1.23**	**0.8**	**1**	**0.79**	**1.3**	**1**	**0.78**	**1.3**	**3**	**3.26**	**0.9**
Esophagus	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Stomach	0	0.07	0.0	1	0.17	6.0	0	0.10	0.0	0	0.10	0.0	1	0.43	2.3
Colon	0	0.21	0.0	0	0.58	0.0	1	0.37	2.7	0	0.38	0.0	1	1.54	0.7
Rectum	0	0.09	0.0	0	0.23	0.0	0	0.15	0.0	1	0.14	7.0	1	0.61	1.6
Liver, biliary	0	0.03	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Pancreas	0	0.05	0.0	0	0.12	0.0	0	0.08	0.0	0	0.08	0.0	0	0.33	0.0
Respiratory system	**0**	**0.09**	**0.0**	**2**	**0.24**	**8.2**	**1**	**0.17**	**6.0**	**0**	**0.16**	**0.0**	**3**	**0.66**	**4.6**
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Larynx	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Trachea, bronchus, lung	0	0.08	0.0	2	0.22	9.1[b]	1	0.15	6.7	0	0.14	0.0	3	0.59	5.1[b]
Female breast	1	0.39	2.6	3	1.02	2.9	2	0.66	3.0	0	0.59	0.0	6	2.66	2.3
Female genital tract	**0**	**0.25**	**0.0**	**1**	**0.62**	**1.6**	**0**	**0.40**	**0.0**	**1**	**0.34**	**2.9**	**2**	**1.61**	**1.2**
Cervix uteri	0	0.05	0.0	0	0.12	0.0	0	0.07	0.0	0	0.06	0.0	0	0.30	0.0
Corpus uteri	0	0.10	0.0	0	0.25	0.0	0	0.17	0.0	1	0.15	6.9	1	0.66	1.5
Uterus, NOS	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.11	0.0
Ovary, fallopian tubes	0	0.07	0.0	1	0.17	5.8	0	0.11	0.0	0	0.09	0.0	1	0.44	2.3
Kidney, renal pelvis, ureter	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Bladder, other urinary	0	0.04	0.0	0	0.11	0.0	0	0.07	0.0	0	0.08	0.0	0	0.30	0.0
Melanoma of the skin	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.12	0.0
Eye	0	0.00	0.0	1	0.01	140.2[b]	0	0.00	0.0	0	0.00	0.0	1	0.02	55.0
Brain, central nervous system	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.10	0.0
Thyroid gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Bone	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Connective tissue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Lymphatic, hematopoietic system	**0**	**0.09**	**0.0**	**1**	**0.25**	**4.0**	**1**	**0.16**	**6.2**	**0**	**0.16**	**0.0**	**2**	**0.67**	**3.0**
Non-Hodgkin's lymphoma	0	0.04	0.0	1	0.10	10.5	1	0.06	16.2	0	0.06	0.0	2	0.25	7.9
Hodgkin's disease	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Multiple myeloma	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Leukemias	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.25	0.0
Chronic lymphocytic	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Acute nonlymphocytic	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0

[a] ICD-O code = 160.

[b] $P < .05$.

LARYNX
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the larynx, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	3,653	486	4,139
No. who developed a second primary cancer	496	45	541
Average age at diagnosis of first cancer, yr	62	59	61
Average yr of diagnosis of first cancer	1965	1970	1966
Person-yr of follow-up	19,528	2,603	22,131
Average follow-up, yr	5.3	5.4	5.3
Percent given radiotherapy for first cancer	58.6	64.6	59.3

[a] ICD-O code = 161.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the larynx in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	476	88.0
Only the first cancer	45	8.3
Only the second cancer	14	2.6
Neither first nor second cancer	6	1.1
Total second primary cancers	541	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LARYNX
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the larynx among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,139			3,217			1,596			782			4,139		
Person-yr in interval	3,020			8,842			5,669			4,600			22,131		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**63**	**34.39**	**1.8**[b]	**208**	**109.94**	**1.9**[b]	**129**	**83.30**	**1.5**[b]	**141**	**86.76**	**1.6**[b]	**541**	**314.21**	**1.7**[b]
All excluding site of initial cancer	**62**	**33.54**	**1.8**[b]	**207**	**107.32**	**1.9**[b]	**129**	**81.47**	**1.6**[b]	**141**	**85.15**	**1.7**[b]	**539**	**307.31**	**1.8**[b]
Buccal cavity, pharynx	**7**	**1.79**	**3.9**[b]	**13**	**5.48**	**2.4**[b]	**12**	**3.86**	**3.1**[b]	**8**	**3.52**	**2.3**	**40**	**14.65**	**2.7**[b]
Lip	0	0.30	0.0	0	0.89	0.0	0	0.63	0.0	0	0.58	0.0	0	2.40	0.0
Tongue	3	0.37	8.2[b]	3	1.11	2.7	4	0.78	5.2[b]	1	0.69	1.5	11	2.94	3.7[b]
Salivary gland	0	0.09	0.0	0	0.27	0.0	0	0.20	0.0	1	0.21	4.8	1	0.77	1.3
Gum, other mouth	2	0.51	3.9	6	1.57	3.8[b]	5	1.10	4.5[b]	0	1.01	0.0	13	4.18	3.1[b]
Pharynx	2	0.46	4.3	3	1.43	2.1	2	1.00	2.0	5	0.89	5.6[b]	12	3.78	3.2[b]
Digestive system	**19**	**10.81**	**1.8**[b]	**47**	**34.11**	**1.4**[b]	**39**	**25.75**	**1.5**[b]	**40**	**26.77**	**1.5**[b]	**145**	**97.38**	**1.5**[b]
Esophagus	4	0.75	5.3[b]	4	2.30	1.7	9	1.64	5.5[b]	2	1.52	1.3	19	6.21	3.1[b]
Stomach	2	1.95	1.0	6	5.85	1.0	8	4.24	1.9	7	4.20	1.7	23	16.23	1.4
Colon	7	3.96	1.8	21	12.83	1.6[b]	13	10.01	1.3	16	10.98	1.5	57	37.76	1.5[b]
Rectum	0	2.29	0.0	7	7.25	1.0	3	5.41	0.6	9	5.47	1.6	19	20.40	0.9
Liver, biliary	1	0.56	1.8	5	1.76	2.8	2	1.34	1.5	2	1.41	1.4	10	5.07	2.0
Pancreas	3	1.11	2.7	4	3.53	1.1	4	2.68	1.5	3	2.77	1.1	14	10.08	1.4
Respiratory system	**17**	**7.06**	**2.4**[b]	**79**	**22.89**	**3.5**[b]	**41**	**17.04**	**2.4**[b]	**45**	**16.71**	**2.7**[b]	**182**	**63.66**	**2.9**[b]
Nasal cavities, sinuses	0	0.07	0.0	2	0.23	8.6	0	0.17	0.0	0	0.17	0.0	2	0.65	3.1
Larynx	1	0.85	1.2	1	2.62	0.4	0	1.83	0.0	0	1.61	0.0	2	6.90	0.3
Trachea, bronchus, lung	16	6.08	2.6[b]	76	19.84	3.8[b]	41	14.89	2.8[b]	45	14.78	3.0[b]	178	55.55	3.2[b]
Female breast	2	0.78	2.6	3	2.31	1.3	2	1.59	1.3	2	1.57	1.3	9	6.24	1.4
Female genital tract	**1**	**0.48**	**2.1**	**1**	**1.41**	**0.7**	**0**	**0.96**	**0.0**	**2**	**0.90**	**2.2**	**4**	**3.75**	**1.1**
Cervix uteri	0	0.09	0.0	1	0.25	4.0	0	0.16	0.0	1	0.13	7.7	2	0.63	3.2
Corpus uteri	0	0.22	0.0	0	0.65	0.0	0	0.45	0.0	0	0.43	0.0	0	1.75	0.0
Uterus, NOS	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.03	0.0	0	0.14	0.0
Ovary, fallopian tubes	1	0.13	7.5	0	0.39	0.0	0	0.27	0.0	1	0.25	4.0	2	1.04	1.9
Prostate gland	6	5.10	1.2	21	17.01	1.2	18	14.07	1.3	18	16.61	1.1	63	52.76	1.2
Testis	0	0.06	0.0	0	0.17	0.0	0	0.10	0.0	0	0.07	0.0	0	0.39	0.0
Kidney, renal pelvis, ureter	4	0.88	4.5[b]	3	2.80	1.1	1	2.06	0.5	3	2.02	1.5	11	7.77	1.4
Bladder, other urinary	1	2.30	0.4	16	7.49	2.1[b]	2	5.82	0.3	9	6.32	1.4	28	21.91	1.3
Melanoma of the skin	1	0.41	2.4	3	1.29	2.3	2	0.92	2.2	1	0.88	1.1	7	3.49	2.0
Eye	1	0.05	18.4	0	0.17	0.0	0	0.12	0.0	0	0.11	0.0	1	0.45	2.2
Brain, central nervous system	0	0.41	0.0	3	1.29	2.3	1	0.88	1.1	2	0.76	2.6	6	3.34	1.8
Thyroid gland	0	0.12	0.0	1	0.35	2.8	0	0.24	0.0	0	0.21	0.0	1	0.92	1.1
Bone	0	0.05	0.0	0	0.15	0.0	0	0.10	0.0	0	0.10	0.0	0	0.40	0.0
Connective tissue	0	0.17	0.0	0	0.53	0.0	0	0.39	0.0	0	0.40	0.0	0	1.48	0.0
Lymphatic, hematopoietic system	**3**	**2.25**	**1.3**	**9**	**7.20**	**1.2**	**7**	**5.43**	**1.3**	**7**	**5.72**	**1.2**	**26**	**20.59**	**1.3**
Non-Hodgkin's lymphoma	1	0.77	1.3	5	2.45	2.0	2	1.80	1.1	3	1.82	1.6	11	6.83	1.6
Hodgkin's disease	0	0.18	0.0	0	0.53	0.0	1	0.36	2.8	0	0.32	0.0	1	1.38	0.7
Multiple myeloma	0	0.34	0.0	0	1.11	0.0	0	0.87	0.0	2	0.95	2.1	2	3.27	0.6
Leukemias	2	0.97	2.1	4	3.11	1.3	4	2.41	1.7	2	2.64	0.8	12	9.11	1.3
Chronic lymphocytic	1	0.31	3.2	1	1.01	1.0	2	0.80	2.5	0	0.88	0.0	4	2.99	1.3
Acute nonlymphocytic	0	0.28	0.0	3	0.92	3.3	1	0.73	1.4	1	0.85	1.2	5	2.78	1.8

[a] ICD-O code = 161.

[b] $P < .05$.

LARYNX
MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the larynx among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,653			2,836			1,417			692			3,653		
Person-yr in interval	2,665			7,819			5,009			4,035			19,528		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**55**	**31.62**	**1.7^b**	**188**	**101.73**	**1.8^b**	**121**	**77.49**	**1.6^b**	**132**	**80.69**	**1.6^b**	**496**	**291.36**	**1.7^b**
All excluding site of initial cancer	**54**	**30.79**	**1.8^b**	**187**	**99.15**	**1.9^b**	**121**	**75.69**	**1.6^b**	**132**	**79.11**	**1.7^b**	**494**	**284.57**	**1.7^b**
Buccal cavity, pharynx	**7**	**1.74**	**4.0^b**	**12**	**5.32**	**2.3^b**	**10**	**3.75**	**2.7^b**	**8**	**3.40**	**2.4^b**	**37**	**14.20**	**2.6^b**
Lip	0	0.30	0.0	0	0.88	0.0	0	0.63	0.0	0	0.58	0.0	0	2.38	0.0
Tongue	3	0.35	8.5^b	3	1.08	2.8	3	0.75	4.0	1	0.66	1.5	10	2.85	3.5^b
Salivary gland	0	0.08	0.0	0	0.25	0.0	0	0.19	0.0	1	0.20	5.1	1	0.72	1.4
Gum, other mouth	2	0.49	4.1	5	1.51	3.3^b	4	1.06	3.8^b	0	0.96	0.0	11	4.02	2.7^b
Pharynx	2	0.45	4.5	3	1.39	2.2	2	0.97	2.1	5	0.86	5.8^b	12	3.67	3.3^b
Digestive system	**15**	**10.09**	**1.5**	**43**	**31.97**	**1.3**	**38**	**24.17**	**1.6^b**	**38**	**24.96**	**1.5^b**	**134**	**91.14**	**1.5^b**
Esophagus	2	0.73	2.7	4	2.25	1.8	9	1.60	5.6^b	2	1.47	1.4	17	6.05	2.8^b
Stomach	2	1.87	1.1	6	5.62	1.1	8	4.08	2.0	6	4.02	1.5	22	15.57	1.4
Colon	5	3.62	1.4	18	11.81	1.5	12	9.25	1.3	16	10.10	1.6	51	34.75	1.5^b
Rectum	0	2.15	0.0	7	6.81	1.0	3	5.09	0.6	8	5.12	1.6	18	19.15	0.9
Liver, biliary	1	0.51	1.9	5	1.63	3.1	2	1.24	1.6	2	1.30	1.5	10	4.68	2.1^b
Pancreas	3	1.03	2.9	3	3.30	0.9	4	2.51	1.6	3	2.57	1.2	13	9.41	1.4
Respiratory system	**17**	**6.84**	**2.5^b**	**72**	**22.23**	**3.2^b**	**39**	**16.57**	**2.4^b**	**44**	**16.23**	**2.7^b**	**172**	**61.82**	**2.8^b**
Nasal cavities, sinuses	0	0.07	0.0	2	0.22	9.2^b	0	0.16	0.0	0	0.16	0.0	2	0.61	3.3
Larynx	1	0.83	1.2	1	2.58	0.4	0	1.80	0.0	0	1.58	0.0	2	6.79	0.3
Trachea, bronchus, lung	16	5.88	2.7^b	69	19.23	3.6^b	39	14.46	2.7^b	44	14.34	3.1^b	168	53.87	3.1^b
Prostate gland	6	5.10	1.2	21	17.01	1.2	18	14.07	1.3	18	16.61	1.1	63	52.76	1.2
Testis	0	0.06	0.0	0	0.17	0.0	0	0.10	0.0	0	0.07	0.0	0	0.39	0.0
Kidney, renal pelvis, ureter	3	0.84	3.6	3	2.67	1.1	1	1.97	0.5	3	1.92	1.6	10	7.40	1.4
Bladder, other urinary	1	2.23	0.4	15	7.28	2.1^b	2	5.67	0.4	9	6.14	1.5	27	21.30	1.3
Melanoma of the skin	1	0.37	2.7	3	1.17	2.6	2	0.84	2.4	1	0.81	1.2	7	3.18	2.2
Eye	1	0.05	20.0	0	0.15	0.0	0	0.11	0.0	0	0.10	0.0	1	0.41	2.4
Brain, central nervous system	0	0.38	0.0	3	1.19	2.5	1	0.81	1.2	1	0.70	1.4	5	3.08	1.6
Thyroid gland	0	0.09	0.0	1	0.29	3.5	0	0.20	0.0	0	0.17	0.0	1	0.75	1.3
Bone	0	0.05	0.0	0	0.14	0.0	0	0.10	0.0	0	0.09	0.0	0	0.38	0.0
Connective tissue	0	0.16	0.0	0	0.50	0.0	0	0.37	0.0	0	0.37	0.0	0	1.39	0.0
Lymphatic, hematopoietic system	**3**	**2.08**	**1.4**	**8**	**6.69**	**1.2**	**6**	**5.06**	**1.2**	**7**	**5.30**	**1.3**	**24**	**19.11**	**1.3**
Non-Hodgkin's lymphoma	1	0.70	1.4	4	2.24	1.8	2	1.64	1.2	3	1.66	1.8	10	6.23	1.6
Hodgkin's disease	0	0.16	0.0	0	0.49	0.0	1	0.34	3.0	0	0.29	0.0	1	1.28	0.8
Multiple myeloma	0	0.31	0.0	0	1.02	0.0	0	0.80	0.0	2	0.86	2.3	2	2.99	0.7
Leukemias	2	0.91	2.2	4	2.93	1.4	3	2.28	1.3	2	2.48	0.8	11	8.60	1.3
Chronic lymphocytic	1	0.29	3.4	1	0.96	1.0	2	0.76	2.6	0	0.83	0.0	4	2.84	1.4
Acute nonlymphocytic	0	0.26	0.0	3	0.86	3.5	0	0.68	0.0	1	0.80	1.3	4	2.59	1.5

[a] ICD-O code = 161.

[b] $P < .05$.

LARYNX
FEMALES

TABLE 2E. –*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the larynx among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	486			381			179			90			486		
Person-yr in interval	355			1,023			660			566			2,603		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8**	**2.77**	**2.9**[b]	**20**	**8.21**	**2.4**[b]	**8**	**5.81**	**1.4**	**9**	**6.07**	**1.5**	**45**	**22.85**	**2.0**[b]
All excluding site of initial cancer	**8**	**2.76**	**2.9**[b]	**20**	**8.17**	**2.4**[b]	**8**	**5.78**	**1.4**	**9**	**6.04**	**1.5**	**45**	**22.74**	**2.0**[b]
Buccal cavity, pharynx	**0**	**0.05**	**0.0**	**1**	**0.16**	**6.2**	**2**	**0.11**	**17.7**[b]	**0**	**0.12**	**0.0**	**3**	**0.45**	**6.7**[b]
Lip	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0
Tongue	0	0.01	0.0	0	0.03	0.0	1	0.02	43.4	0	0.02	0.0	1	0.09	11.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Gum, other mouth	0	0.02	0.0	1	0.06	17.7	1	0.04	25.3	0	0.04	0.0	2	0.16	12.8[b]
Pharynx	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Digestive system	**4**	**0.72**	**5.6**[b]	**4**	**2.15**	**1.9**	**1**	**1.58**	**0.6**	**2**	**1.80**	**1.1**	**11**	**6.24**	**1.8**
Esophagus	2	0.02	104.1[b]	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	2	0.16	12.4[b]
Stomach	0	0.08	0.0	0	0.23	0.0	0	0.16	0.0	1	0.18	5.4	1	0.65	1.5
Colon	2	0.34	5.9	3	1.02	2.9	1	0.76	1.3	0	0.89	0.0	6	3.01	2.0
Rectum	0	0.15	0.0	0	0.44	0.0	0	0.32	0.0	1	0.35	2.9	1	1.26	0.8
Liver, biliary	0	0.04	0.0	0	0.13	0.0	0	0.10	0.0	0	0.11	0.0	0	0.38	0.0
Pancreas	0	0.07	0.0	1	0.23	4.4	0	0.17	0.0	0	0.19	0.0	1	0.66	1.5
Respiratory system	**0**	**0.22**	**0.0**	**7**	**0.66**	**10.6**[b]	**2**	**0.47**	**4.2**	**1**	**0.48**	**2.1**	**10**	**1.84**	**5.4**[b]
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Trachea, bronchus, lung	0	0.20	0.0	7	0.60	11.7[b]	2	0.43	4.6	1	0.44	2.3	10	1.67	6.0[b]
Female breast	2	0.78	2.6	3	2.31	1.3	2	1.59	1.3	2	1.57	1.3	9	6.24	1.4
Female genital tract	**1**	**0.48**	**2.1**	**1**	**1.41**	**0.7**	**0**	**0.96**	**0.0**	**2**	**0.90**	**2.2**	**4**	**3.75**	**1.1**
Cervix uteri	0	0.09	0.0	1	0.25	4.0	0	0.16	0.0	1	0.13	7.7	2	0.63	3.2
Corpus uteri	0	0.22	0.0	0	0.65	0.0	0	0.45	0.0	0	0.43	0.0	0	1.75	0.0
Uterus, NOS	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.03	0.0	0	0.14	0.0
Ovary, fallopian tubes	1	0.13	7.5	0	0.39	0.0	0	0.27	0.0	1	0.25	4.0	2	1.04	1.9
Kidney, renal pelvis, ureter	1	0.04	22.8	0	0.13	0.0	0	0.10	0.0	0	0.10	0.0	1	0.37	2.7
Bladder, other urinary	0	0.07	0.0	1	0.21	4.7	0	0.16	0.0	0	0.18	0.0	1	0.62	1.6
Melanoma of the skin	0	0.04	0.0	0	0.12	0.0	0	0.08	0.0	0	0.07	0.0	0	0.31	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Brain, central nervous system	0	0.03	0.0	0	0.10	0.0	0	0.07	0.0	1	0.06	16.0	1	0.26	3.8
Thyroid gland	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Bone	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Lymphatic, hematopoietic system	**0**	**0.17**	**0.0**	**1**	**0.52**	**1.9**	**1**	**0.37**	**2.7**	**0**	**0.42**	**0.0**	**2**	**1.48**	**1.3**
Non-Hodgkin's lymphoma	0	0.07	0.0	1	0.21	4.7	0	0.15	0.0	0	0.17	0.0	1	0.60	1.7
Hodgkin's disease	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.10	0.0
Multiple myeloma	0	0.03	0.0	0	0.09	0.0	0	0.07	0.0	0	0.08	0.0	0	0.27	0.0
Leukemias	0	0.06	0.0	0	0.17	0.0	1	0.13	7.9	0	0.15	0.0	1	0.51	2.0
Chronic lymphocytic	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.05	0.0	0	0.15	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.06	0.0	1	0.05	21.4	0	0.06	0.0	1	0.19	5.3

[a] ICD-O code = 161.

[b] $P < .05$.

LUNG
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TABLE 3A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the trachea, bronchus, or lung, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	18,764	5,659	24,423
No. who developed a second primary cancer	485	129	614
Average age at diagnosis of first cancer, yr	63	61	62
Average yr of diagnosis of first cancer	1969	1972	1970
Person-yr of follow-up	23,669	8,736	32,405
Average follow-up, yr	1.3	1.5	1.3
Percent given radiotherapy for first cancer	56.1	54.0	55.6

[a] ICD-O code = 162.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the trachea, bronchus, or lung in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	536	87.3
Only the first cancer	45	7.3
Only the second cancer	22	3.6
Neither first nor second cancer	11	1.8
Total second primary cancers	614	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

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TABLE 3C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the trachea, bronchus, or lung among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	24,423			8,504			1,636			577			24,423		
Person-yr in interval	11,368			13,408			4,992			2,636			32,405		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**195**	**140.76**	**1.4**[b]	**237**	**172.11**	**1.4**[b]	**114**	**69.58**	**1.6**[b]	**68**	**44.28**	**1.5**[b]	**614**	**426.38**	**1.4**[b]
All excluding site of initial cancer	**183**	**116.01**	**1.6**[b]	**192**	**141.80**	**1.4**[b]	**80**	**57.34**	**1.4**[b]	**49**	**36.74**	**1.3**	**504**	**351.61**	**1.4**[b]
Buccal cavity, pharynx	**20**	**6.26**	**3.2**[b]	**16**	**7.34**	**2.2**[b]	**8**	**2.84**	**2.8**[b]	**2**	**1.63**	**1.2**	**46**	**18.06**	**2.5**[b]
Lip	0	0.90	0.0	2	1.00	2.0	2	0.38	5.3	0	0.22	0.0	4	2.50	1.6
Tongue	8	1.26	6.4[b]	2	1.47	1.4	1	0.57	1.8	0	0.32	0.0	11	3.61	3.0[b]
Salivary gland	3	0.34	8.8[b]	1	0.40	2.5	0	0.16	0.0	0	0.10	0.0	4	1.00	4.0[b]
Gum, other mouth	4	1.84	2.2	4	2.19	1.8	2	0.85	2.3	0	0.49	0.0	10	5.36	1.9
Pharynx	4	1.67	2.4	7	1.97	3.5[b]	3	0.76	3.9	2	0.43	4.7	16	4.83	3.3[b]
Digestive system	**56**	**42.01**	**1.3**[b]	**55**	**50.75**	**1.1**	**24**	**20.52**	**1.2**	**16**	**13.21**	**1.2**	**151**	**126.37**	**1.2**[b]
Esophagus	5	2.59	1.9	1	3.04	0.3	3	1.19	2.5	1	0.69	1.4	10	7.50	1.3
Stomach	9	6.39	1.4	10	7.36	1.4	4	2.90	1.4	4	1.80	2.2	27	18.43	1.5
Colon	16	16.77	1.0	23	20.68	1.1	9	8.49	1.1	5	5.68	0.9	53	51.58	1.0
Rectum	12	8.91	1.3	13	10.75	1.2	8	4.33	1.8	3	2.74	1.1	36	26.70	1.3
Liver, biliary	2	2.23	0.9	1	2.72	0.4	0	1.10	0.0	0	0.70	0.0	3	6.75	0.4
Pancreas	10	4.40	2.3[b]	7	5.34	1.3	0	2.17	0.0	3	1.38	2.2	20	13.29	1.5
Respiratory system	**17**	**28.29**	**0.6**[b]	**51**	**34.52**	**1.5**[b]	**38**	**13.89**	**2.7**[b]	**19**	**8.48**	**2.2**[b]	**125**	**85.11**	**1.5**[b]
Nasal cavities, sinuses	1	0.28	3.5	0	0.34	0.0	0	0.13	0.0	0	0.08	0.0	1	0.84	1.2
Larynx	4	2.99	1.3	6	3.55	1.7	4	1.39	2.9	0	0.78	0.0	14	8.71	1.6
Trachea, bronchus, lung	12	24.75	0.5[b]	45	30.31	1.5[b]	34	12.24	2.8[b]	19	7.54	2.5[b]	110	74.77	1.5[b]
Female breast	7	6.87	1.0	13	9.28	1.4	5	3.75	1.3	5	2.25	2.2	30	22.13	1.4
Female genital tract	**7**	**4.03**	**1.7**	**4**	**5.40**	**0.7**	**3**	**2.17**	**1.4**	**1**	**1.26**	**0.8**	**15**	**12.85**	**1.2**
Cervix uteri	0	0.64	0.0	1	0.82	1.2	2	0.32	6.2	1	0.17	5.7	4	1.95	2.0
Corpus uteri	3	1.94	1.5	1	2.64	0.4	1	1.08	0.9	0	0.62	0.0	5	6.27	0.8
Uterus, NOS	0	0.14	0.0	0	0.17	0.0	0	0.06	0.0	0	0.04	0.0	0	0.40	0.0
Ovary, fallopian tubes	3	1.11	2.7	2	1.49	1.3	0	0.60	0.0	0	0.35	0.0	5	3.55	1.4
Prostate gland	46	19.68	2.3[b]	54	23.92	2.3[b]	12	9.99	1.2	9	7.05	1.3	121	60.60	2.0[b]
Testis	0	0.19	0.0	0	0.21	0.0	0	0.07	0.0	0	0.03	0.0	0	0.50	0.0
Kidney, renal pelvis, ureter	12	3.47	3.5[b]	14	4.20	3.3[b]	1	1.68	0.6	0	1.03	0.0	27	10.37	2.6[b]
Bladder, other urinary	8	9.12	0.9	11	11.14	1.0	7	4.54	1.5	8	3.00	2.7[b]	34	27.78	1.2
Melanoma of the skin	1	1.79	0.6	1	2.21	0.5	3	0.86	3.5	0	0.50	0.0	5	5.35	0.9
Eye	0	0.21	0.0	1	0.25	4.1	0	0.10	0.0	0	0.06	0.0	1	0.61	1.6
Brain, central nervous system	1	1.68	0.6	1	2.04	0.5	1	0.79	1.3	0	0.44	0.0	3	4.94	0.6
Thyroid gland	4	0.50	7.9[b]	0	0.62	0.0	0	0.24	0.0	0	0.13	0.0	4	1.49	2.7
Bone	0	0.18	0.0	0	0.21	0.0	0	0.08	0.0	0	0.05	0.0	0	0.51	0.0
Connective tissue	2	0.65	3.1	1	0.79	1.3	1	0.31	3.2	0	0.19	0.0	4	1.94	2.1
Lymphatic, hematopoietic system	**7**	**9.32**	**0.8**	**7**	**11.39**	**0.6**	**8**	**4.60**	**1.7**	**5**	**2.96**	**1.7**	**27**	**28.24**	**1.0**
Non-Hodgkin's lymphoma	3	3.27	0.9	1	4.04	0.2	2	1.62	1.2	2	1.00	2.0	8	9.93	0.8
Hodgkin's disease	0	0.65	0.0	2	0.76	2.6	0	0.29	0.0	0	0.17	0.0	2	1.87	1.1
Multiple myeloma	2	1.51	1.3	0	1.88	0.0	2	0.77	2.6	0	0.51	0.0	4	4.67	0.9
Leukemias	2	3.88	0.5	4	4.70	0.9	4	1.92	2.1	3	1.28	2.4	13	11.76	1.1
Chronic lymphocytic	0	1.26	0.0	2	1.53	1.3	1	0.63	1.6	1	0.42	2.4	4	3.84	1.0
Acute nonlymphocytic	2	1.25	1.6	2	1.56	1.3	3	0.65	4.6	1	0.45	2.2	8	3.90	2.1

[a] ICD-O code = 162.

[b] $P < .05$.

LUNG
MALES

TABLE 3D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the trachea, bronchus, or lung among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	18,764			6,330			1,171			414			18,764		
Person-yr in interval	8,581			9,697			3,548			1,843			23,669		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**154**	**115.67**	**1.3**[b]	**184**	**138.01**	**1.3**[b]	**94**	**55.65**	**1.7**[b]	**53**	**35.57**	**1.5**[b]	**485**	**344.60**	**1.4**[b]
All excluding site of initial cancer	**147**	**92.91**	**1.6**[b]	**152**	**110.45**	**1.4**[b]	**65**	**44.55**	**1.5**[b]	**37**	**28.73**	**1.3**	**401**	**276.40**	**1.5**[b]
Buccal cavity, pharynx	**18**	**5.76**	**3.1**[b]	**13**	**6.66**	**2.0**[b]	**7**	**2.56**	**2.7**[b]	**2**	**1.47**	**1.4**	**40**	**16.43**	**2.4**[b]
Lip	0	0.88	0.0	2	0.97	2.1	2	0.37	5.4	0	0.21	0.0	4	2.43	1.6
Tongue	7	1.15	6.1[b]	2	1.33	1.5	0	0.51	0.0	0	0.29	0.0	9	3.28	2.7[b]
Salivary gland	3	0.29	10.4[b]	1	0.34	3.0	0	0.13	0.0	0	0.08	0.0	4	0.84	4.8[b]
Gum, other mouth	4	1.66	2.4	2	1.94	1.0	2	0.75	2.7	0	0.43	0.0	8	4.78	1.7
Pharynx	3	1.54	1.9	6	1.80	3.3[b]	3	0.69	4.3	2	0.39	5.1	14	4.43	3.2[b]
Digestive system	**48**	**35.26**	**1.4**[b]	**44**	**41.52**	**1.1**	**21**	**16.69**	**1.3**	**13**	**10.65**	**1.2**	**126**	**104.03**	**1.2**[b]
Esophagus	4	2.41	1.7	1	2.79	0.4	3	1.08	2.8	1	0.63	1.6	9	6.90	1.3
Stomach	9	5.71	1.6	9	6.44	1.4	3	2.52	1.2	4	1.54	2.6	25	16.20	1.5
Colon	15	13.50	1.1	17	16.20	1.0	8	6.63	1.2	4	4.41	0.9	44	40.71	1.1
Rectum	8	7.55	1.1	10	8.90	1.1	7	3.56	2.0	2	2.24	0.9	27	22.23	1.2
Liver, biliary	1	1.83	0.5	0	2.17	0.0	0	0.87	0.0	0	0.55	0.0	1	5.41	0.2
Pancreas	9	3.67	2.4[b]	7	4.35	1.6	0	1.75	0.0	2	1.10	1.8	18	10.87	1.7
Respiratory system	**10**	**26.11**	**0.4**[b]	**36**	**31.50**	**1.1**	**33**	**12.65**	**2.6**[b]	**16**	**7.73**	**2.1**[b]	**95**	**77.92**	**1.2**
Nasal cavities, sinuses	0	0.24	0.0	0	0.28	0.0	0	0.11	0.0	0	0.07	0.0	0	0.70	0.0
Larynx	3	2.87	1.0	4	3.38	1.2	4	1.32	3.0	0	0.74	0.0	11	8.30	1.3
Trachea, bronchus, lung	7	22.76	0.3[b]	32	27.56	1.2	29	11.10	2.6[b]	16	6.84	2.3[b]	84	68.20	1.2
Prostate gland	46	19.68	2.3[b]	54	23.92	2.3[b]	12	9.99	1.2	9	7.05	1.3	121	60.60	2.0[b]
Testis	0	0.19	0.0	0	0.21	0.0	0	0.07	0.0	0	0.03	0.0	0	0.50	0.0
Kidney, renal pelvis, ureter	8	3.06	2.6[b]	11	3.65	3.0[b]	1	1.45	0.7	0	0.88	0.0	20	9.03	2.2[b]
Bladder, other urinary	7	8.44	0.8	11	10.18	1.1	7	4.15	1.7	8	2.73	2.9[b]	33	25.48	1.3
Melanoma of the skin	1	1.43	0.7	1	1.73	0.6	2	0.67	3.0	0	0.39	0.0	4	4.22	0.9
Eye	0	0.17	0.0	1	0.20	5.1	0	0.08	0.0	0	0.04	0.0	1	0.49	2.1
Brain, central nervous system	1	1.39	0.7	1	1.64	0.6	1	0.63	1.6	0	0.35	0.0	3	4.00	0.8
Thyroid gland	3	0.32	9.2[b]	0	0.38	0.0	0	0.14	0.0	0	0.08	0.0	3	0.92	3.3
Bone	0	0.15	0.0	0	0.17	0.0	0	0.06	0.0	0	0.04	0.0	0	0.42	0.0
Connective tissue	2	0.56	3.6	1	0.65	1.5	1	0.26	3.9	0	0.16	0.0	4	1.63	2.5
Lymphatic, hematopoietic system	**4**	**7.69**	**0.5**	**7**	**9.16**	**0.8**	**6**	**3.69**	**1.6**	**4**	**2.35**	**1.7**	**21**	**22.86**	**0.9**
Non-Hodgkin's lymphoma	2	2.60	0.8	1	3.12	0.3	1	1.23	0.8	1	0.76	1.3	5	7.70	0.6
Hodgkin's disease	0	0.55	0.0	2	0.62	3.2	0	0.24	0.0	0	0.14	0.0	2	1.54	1.3
Multiple myeloma	1	1.21	0.8	0	1.46	0.0	1	0.60	1.7	0	0.39	0.0	2	3.66	0.5
Leukemias	1	3.33	0.3	4	3.96	1.0	4	1.61	2.5	3	1.07	2.8	12	9.96	1.2
Chronic lymphocytic	0	1.10	0.0	2	1.31	1.5	1	0.54	1.9	1	0.36	2.8	4	3.30	1.2
Acute nonlymphocytic	1	1.04	1.0	2	1.27	1.6	3	0.54	5.6[b]	1	0.37	2.7	7	3.21	2.2

[a] ICD-O code = 162.

[b] $P < .05$.

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TABLE 3E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the trachea, bronchus, or lung among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,659			2,174			465			163			5,659		
Person-yr in interval	2,787			3,711			1,444			793			8,736		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**41**	**25.09**	**1.6^b**	**53**	**34.10**	**1.6^b**	**20**	**13.93**	**1.4**	**15**	**8.71**	**1.7**	**129**	**81.77**	**1.6^b**
All excluding site of initial cancer	**36**	**23.10**	**1.6^b**	**40**	**31.34**	**1.3**	**15**	**12.80**	**1.2**	**12**	**8.02**	**1.5**	**103**	**75.20**	**1.4^b**
Buccal cavity, pharynx	**2**	**0.50**	**4.0**	**3**	**0.68**	**4.4**	**1**	**0.28**	**3.5**	**0**	**0.17**	**0.0**	**6**	**1.63**	**3.7^b**
Lip	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Tongue	1	0.10	9.7	0	0.14	0.0	1	0.06	17.3	0	0.03	0.0	2	0.33	6.0
Salivary gland	0	0.05	0.0	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.17	0.0
Gum, other mouth	0	0.18	0.0	2	0.24	8.2	0	0.10	0.0	0	0.06	0.0	2	0.58	3.4
Pharynx	1	0.12	8.1	1	0.17	5.9	0	0.07	0.0	0	0.04	0.0	2	0.40	5.0
Digestive system	**8**	**6.75**	**1.2**	**11**	**9.22**	**1.2**	**3**	**3.82**	**0.8**	**3**	**2.56**	**1.2**	**25**	**22.34**	**1.1**
Esophagus	1	0.18	5.5	0	0.25	0.0	0	0.10	0.0	0	0.07	0.0	1	0.60	1.7
Stomach	0	0.69	0.0	1	0.92	1.1	1	0.38	2.7	0	0.25	0.0	2	2.23	0.9
Colon	1	3.27	0.3	6	4.48	1.3	1	1.86	0.5	1	1.27	0.8	9	10.87	0.8
Rectum	4	1.36	2.9	3	1.85	1.6	1	0.77	1.3	1	0.50	2.0	9	4.47	2.0
Liver, biliary	1	0.40	2.5	1	0.55	1.8	0	0.23	0.0	0	0.15	0.0	2	1.34	1.5
Pancreas	1	0.73	1.4	0	1.00	0.0	0	0.42	0.0	1	0.28	3.6	2	2.42	0.8
Respiratory system	**7**	**2.18**	**3.2^b**	**15**	**3.02**	**5.0^b**	**5**	**1.24**	**4.0^b**	**3**	**0.76**	**4.0**	**30**	**7.19**	**4.2^b**
Nasal cavities, sinuses	1	0.04	23.5	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	1	0.14	7.3
Larynx	1	0.13	7.9	2	0.17	11.5^b	0	0.07	0.0	0	0.04	0.0	3	0.41	7.3^b
Trachea, bronchus, lung	5	1.99	2.5	13	2.76	4.7^b	5	1.13	4.4^b	3	0.69	4.3	26	6.57	4.0^b
Female breast	7	6.87	1.0	13	9.28	1.4	5	3.75	1.3	5	2.25	2.2	30	22.13	1.4
Female genital tract	**7**	**4.03**	**1.7**	**4**	**5.40**	**0.7**	**3**	**2.17**	**1.4**	**1**	**1.26**	**0.8**	**15**	**12.85**	**1.2**
Cervix uteri	0	0.64	0.0	1	0.82	1.2	2	0.32	6.2	1	0.17	5.7	4	1.95	2.0
Corpus uteri	3	1.94	1.5	1	2.64	0.4	1	1.08	0.9	0	0.62	0.0	5	6.27	0.8
Uterus, NOS	0	0.14	0.0	0	0.17	0.0	0	0.06	0.0	0	0.04	0.0	0	0.40	0.0
Ovary, fallopian tubes	3	1.11	2.7	2	1.49	1.3	0	0.60	0.0	0	0.35	0.0	5	3.55	1.4
Kidney, renal pelvis, ureter	4	0.41	9.8^b	3	0.56	5.4^b	0	0.23	0.0	0	0.15	0.0	7	1.34	5.2^b
Bladder, other urinary	1	0.69	1.5	0	0.95	0.0	0	0.40	0.0	0	0.26	0.0	1	2.30	0.4
Melanoma of the skin	0	0.35	0.0	0	0.48	0.0	1	0.19	5.3	0	0.11	0.0	1	1.13	0.9
Eye	0	0.04	0.0	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.12	0.0
Brain, central nervous system	0	0.29	0.0	0	0.40	0.0	0	0.16	0.0	0	0.09	0.0	0	0.94	0.0
Thyroid gland	1	0.18	5.6	0	0.24	0.0	0	0.09	0.0	0	0.05	0.0	1	0.57	1.8
Bone	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.09	0.0
Connective tissue	0	0.10	0.0	0	0.13	0.0	0	0.05	0.0	0	0.03	0.0	0	0.31	0.0
Lymphatic, hematopoietic system	**3**	**1.63**	**1.8**	**0**	**2.23**	**0.0**	**2**	**0.92**	**2.2**	**1**	**0.60**	**1.7**	**6**	**5.38**	**1.1**
Non-Hodgkin's lymphoma	1	0.67	1.5	0	0.93	0.0	1	0.38	2.6	1	0.25	4.1	3	2.23	1.3
Hodgkin's disease	0	0.11	0.0	0	0.14	0.0	0	0.06	0.0	0	0.03	0.0	0	0.33	0.0
Multiple myeloma	1	0.30	3.3	0	0.42	0.0	1	0.17	5.8	0	0.12	0.0	2	1.01	2.0
Leukemias	1	0.55	1.8	0	0.74	0.0	0	0.31	0.0	0	0.21	0.0	1	1.80	0.6
Chronic lymphocytic	0	0.16	0.0	0	0.22	0.0	0	0.09	0.0	0	0.07	0.0	0	0.54	0.0
Acute nonlymphocytic	1	0.21	4.8	0	0.29	0.0	0	0.12	0.0	0	0.08	0.0	1	0.69	1.5

[a] ICD-O code = 162.

[b] $P < .05$.

Second Cancer Following Cancer of the Breast in Connecticut, 1935–82 [1]

Elizabeth B. Harvey [2] *and* Louise A. Brinton [3]

ABSTRACT—Among 41,109 women diagnosed with breast cancer between 1935 and 1982 in Connecticut, 3,984 developed a second cancer, whereas 2,426 were expected [relative risk (RR) = 1.64; 95% CI = 1.6–1.7]. This increased risk persisted for 30 years and was highest in women under 55 years of age at the time of breast cancer diagnosis. Second primary breast cancers (RR = 3.0) accounted for almost one-half of all new neoplasms. However, if subsequent breast cancers were excluded, the risk for all other second cancers was only 1.15 (95% CI = 1.10–1.20), and no excess risk was seen among women over age 55 at initial breast cancer. Significant risks were found for cancers of the ovary (RR = 1.7) and uterine corpus (RR = 1.4), possibly linked with shared reproductive factors such as nulliparity or late age at menopause. Malignant melanoma (RR = 1.5), thyroid cancer (RR = 1.6), and colon cancer (RR = 1.2) were also significantly elevated; possible shared risk factors remain to be elucidated. Significant deficits of multiple myeloma and chronic lymphocytic leukemia were noted. Women who received initial radiotherapy compared with those who did not were at slightly higher risk of developing a second cancer, most notably acute nonlymphocytic leukemia, non-Hodgkin's lymphoma, and cancers of the esophagus, kidney, and connective tissue, although the nature of the associations was not always clear. Some of the soft tissue sarcomas were lymphangiosarcomas of the arm, a consequence of the lymphedema that may complicate radical mastectomy (Stewart-Treves syndrome). Women treated with radiation were at higher risk of developing a second breast neoplasm (RR = 3.9) than nonirradiated women (RR = 2.8). Further investigation should focus on the mechanisms underlying the relationships between breast, genital tract, and colon cancers, and on the effects of treatment modalities on the risk of subsequent neoplasms.—Natl Cancer Inst Monogr 68: 99–112, 1985.

The incidence of breast cancer (ICD-O, 174) exceeds that of any other cancer among American women. One of 11 women will develop this disease in their lifetime (*1*). The relatively good survival following an initial diagnosis of breast cancer, i.e., 74% at 5 years, provides ample opportunity for women to develop second primary cancers over time, particularly for sites which may be associated with initial treatment or with common risk factors (e.g., hormonal influences).

Previous studies have demonstrated that women with breast cancer are at a threefold to fourfold excess risk of developing a new primary cancer in the opposite breast (*2–5*). Studies of multiple primary cancers have also reported an excess of thyroid (*5–7*), colon (*2, 8*), ovarian (*5, 7–10*), uterine (*5, 7, 8, 11, 12*), and connective tissue (*5, 8*) neoplasms, as well as melanoma (*13, 14*) following breast cancer. Factors suggested to explain these associations include genetic influences, common environmental exposures, endogenous hormones, increased medical surveillance among cancer patients, and treatments for the initial primary cancer. An excess risk of cancer of the uterine corpus has been associated with nonsteroidal estrogen treatment for breast cancer (*15*) and ovarian radiotherapy (*16*). An excess of leukemia following chemotherapy (*17, 18*) and second breast cancers after radiotherapy (*19*) have also been reported.

RESULTS

A total of 41,109 women developed breast cancer in Connecticut between 1935 and 1982. The average age at breast cancer diagnosis was 59 years, and the average follow-up was 6.6 years. Overall, 3,984 (or 10%) of these women developed a second cancer versus 2,426 expected (RR = 1.64; 95% CI = 1.6–1.7). A significantly elevated risk was found for second breast cancer (3.0), which accounted for 48% of all second tumors. Excluding breast cancer as a second cancer, the overall risk for developing a subsequent neoplasm was only slightly elevated (RR = 1.15; 95% CI = 1.10–1.20). However, significant excesses were seen for cancers of the colon (RR = 1.2; *n* = 411), lung (RR = 1.3; *n* = 177), uterine corpus (RR = 1.4; *n* = 227), ovary (RR = 1.7; *n* = 183), eye (RR = 2.5; *n* = 10), thyroid (RR = 1.6; *n* = 28), and connective tissue, (RR = 2.3; *n* = 23) and for melanoma (RR = 1.5; *n* = 43). The risk of ANLL was also increased (1.5; 95% CI = 1.0–2.1). Only multiple myeloma (RR = 0.5; 95% CI = 0.3–0.9) and CLL (RR = 0.5; 95% CI = 0.2–1.0) were notably decreased below expectation.

Latency

Significant 30 to 70% excesses of second cancers after breast cancer persisted throughout all four decades of observation. The overall pattern of risk over time was heavily influenced by second breast cancer risk which decreased over time but remained elevated (RR = 1.5) even among 30-year survivors. The decreasing RR of second breast cancer, however, was balanced by a significantly increasing RR associated with all other second tumors, most notably cancers of the colon and lung. Other

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ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia; CLL = chronic lymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Radiation Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3A22, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Elizabeth B. Harvey, Ph.D.

[3] Environmental Epidemiology Branch, Division of Cancer Etiology.

than the breast, the only site for which risks decreased significantly over time since diagnosis of the initial primary was cancer of the stomach. Little change over time was seen for cancers of the uterine corpus, cervix, and ovary. Among the 2,661 women with primary breast cancer observed for more than 20 years since diagnosis, 340 total second cancers occurred versus 218 expected (RR = 1.6; 95% CI = 1.4–1.7); when the 115 second breast cancers were excluded, this risk was reduced only slightly (1.4; 95% CI = 1.2–1.5). Cancer sites for which elevations were significant after 20 years of follow-up included the colon (RR = 1.5; *n* = 52), rectum (RR = 1.8; *n* = 24), lung (RR = 2.3; *n* = 32), breast (RR = 2.2; *n* = 115), uterus (RR = 1.6; *n* = 21), ovary (RR = 1.7; *n* = 14), and eye (RR = 5.9; *n* = 2).

Treatment

Radiotherapy was initially given to 28% of the breast cancer patients. The 11,691 women treated with radiation had a slightly greater excess risk of developing a second cancer than did the 29,418 treated by other means (2.0; 95% CI = 1.9–2.1 vs. RR = 1.5; 95% CI = 1.5–1.6). The difference between the 2 groups persisted throughout 20 years posttreatment, after which time the risks were virtually equal (RR = 1.7 vs. 1.5). Women treated with radiation were at higher RR of developing a second breast neoplasm (3.9) than nonirradiated women (2.8). Other second cancers which were significantly more common among women treated with radiation than those not treated with radiation included cancers of the esophagus (RR = 1.7 vs. 0.7), kidney (RR = 1.9 vs. 0.7), and connective tissue (RR = 4.2 vs. 1.8), as well as non-Hodgkin's lymphoma (RR = 1.7 vs. 0.7), CLL (RR = 1.2 vs. 0.4), and ANLL (RR = 2.5 vs. 1.2). Lung cancer risks were significantly elevated among irradiated women 10–19 years (RR = 2.3) and 20–29 years (4.8) posttreatment, with lesser elevations seen in the nonirradiated women (RR = 1.5 and 1.8).

Age

Overall, the risk of a second primary developing was greater in the 6,958 women who were less than 45 years of age at the time of breast cancer diagnosis than in women who were older. This risk decreased with age at breast cancer diagnosis (< 45 yr, RR = 2.9; 45–54 yr, 2.0; 55+ yr, 1.3), as did RR of second breast cancers (5.4, 3.4, and 2.2, respectively). However, when second breast cancers were removed from consideration, the risk of developing other second tumors was present in women under age 45 at initial treatment (RR = 1.5; 95% CI = 1.4–1.7) and in the 9,961 women aged 45 to 54 (1.4; 95% CI = 1.2–1.5), but not among the 24,190 women more than 55 years old (1.0; 95% CI = 0.97–1.1).

Significant downward trends of cancer risk by age at diagnosis were observed for cancers of the ovary (RR = 2.6, 2.4, 1.2), thyroid (3.2, 2.6, 0.6), colon (1.6, 1.3, 1.1), and rectum (1.9, 1.1, 1.0). The risks for lung cancer and malignant melanoma were elevated only among women whose breast cancers were diagnosed before the age of 55 (RR = 1.7 and 2.1, respectively). The risk for uterine corpus cancer, on the other hand, showed an increasing pattern with age at breast cancer diagnosis (RR = 1.1, 1.3, 1.5).

DISCUSSION

Women with primary breast cancer were at a significantly increased risk of developing a second primary cancer, even after 30 years of survival. The largest excess risk observed was the threefold elevation found for second breast cancers; this result is in agreement with previous findings (*4, 5, 19*). In our study, the risk for second breast cancers decreased with time but remained elevated even among women followed over 30 years. The excess risk of second breast cancer was seen in women of all ages at the time of initial breast cancer diagnosis but was highest among those whose breast cancer was diagnosed at an early age. This may reflect a tendency for familial cases of breast cancer to occur at an early age and to be bilateral (*20*). In addition, elevated risks of second primaries of the breast were observed in patients who were treated with and without radiotherapy. Previous studies (*21, 22*) have shown that radiation exposure can result in excess cancer risks to the breast, but the effects were restricted to women exposed under the age of 40 years (*21, 23*). Therefore, it is not surprising that we failed to find clear evidence of a radiation treatment effect for second breast neoplasms. Even though there was a difference in risk of second breast cancers among the irradiated versus the nonirradiated, this mainly reflected a risk difference occurring in the first 5 years of follow-up. Although the minimal latency for radiogenic breast cancer may be on the order of 5–9 years for women over age 30 when irradiated (*23*), the preponderance of excess risk would be expected among those observed for 10 and more years.

Excess risks were found for genital tract cancers, primarily the ovary and uterine corpus, particularly given the large number of cancers and the consistency of the risks with previous studies (*5, 7, 8*). These observations, coupled with the bidirectional associations between these cancers (*11, 24*), strongly suggest the influence of common etiologic factors (*8, 25–27*). Supporting the role of hormonal influences are such shared risk factors as nulliparity and late age at menopause, but other explanations are possible. Although a portion of the excess of ovarian cancer could be mistaken metastases because 9–20% of all breast metastases occur in the ovaries (*28*), the expected value of ovarian cancer is probably underestimated when population rates are used. Treatment for breast cancer often includes removal or radiation ablation of the ovaries. Similarly, the overall increase of uterine corpus cancer is likely an underestimate of the risk in women with intact uteri because hysterectomies are sometimes performed as part of the treatment for breast cancer (*29*). An increased risk of uterine corpus cancer has been reported in women who received nonsteroidal estrogens for treatment of breast cancer (*15*), which could account for some of the excess. Radiation to the ovaries for breast cancer treatment has also been associated with an increased risk of uterine cancer (*16*).

Other relevant second tumors of interest include thyroid cancer and melanoma because breast cancer was also found to be significantly elevated following both these neoplasms in the Connecticut survey (*30*). However, the excess of thyroid cancer after breast cancer, concentrated during the first year of follow-up, might reflect medical surveillance bias. The excess may also be indicative of shared endocrine factors (*6*), although epidemiologic evidence for this explanation is tenuous (*31*). The excess of melanoma deserves attention, inasmuch as bidirectional risks have been reported for these diseases (*30*); the possibility of endocrine factors common to both tumors is also raised (*13*). The role of sex hormones in melanoma development has been suggested by sex differences in survival and incidence, the rarity of melanoma in prepubescent individuals, the effects of pregnancy on melanoma growth (*32*), and a possible influence of oral contraceptives (*33*). In addition, estrogen receptors have been found in malignant melanoma as well as in breast cancer tissues (*34, 35*). The surprising elevation in eye cancer after breast cancer, which was also observed in a previous survey in Connecticut (*8*), is noteworthy; 8 of the 10 cases were intraocular melanomas. Although the choroid of the eye is a common metastatic site for breast cancer (*36*), all cases of melanoma were histologically confirmed.

Cancer of the connective tissue occurred more frequently than expected, and the excess risk persisted throughout the 30-year period of observation and was significantly higher in women who received radiation treatment. A radiation effect is possible, inasmuch as soft tissue sarcomas tend to arise in areas exposed to radiation (*37*). However, the excess was due at least partly to lymphedema of the upper extremities that may accompany radical mastectomy and predispose to lymphangiosarcoma or Stewart-Treves syndrome (*38*). Note that 8 of the 23 connective tissue tumors in this study were lymphangiosarcomas arising from the arms or shoulders.

Our finding of an excess risk of lung cancer confirms a previous survey of breast cancer (*7*). However, the reasons for the association are unclear because smokers are generally thought to be at low risk of developing breast cancer (*39*). Radiation has been previously implicated in the induction of lung cancer (*40*), and the lung receives a substantial dose from the radiotherapy administered for breast cancer. The effect of initial radiotherapy in our study is uncertain, however, because nonexposed women had an equally high risk of developing lung cancer and no precise relationship of risk with years since first treatment with radiation was detected. The excess risk of esophageal cancer in women irradiated for breast cancer is consistent with a previous report of this association (*41*).

The excess risk of ANLL, observed 20 years after initial breast cancer, was more pronounced in the irradiated group and could result from radiotherapy. However, the leukemogenic risk of therapeutic doses of radiation for breast cancer has not been fully clarified. The risk could also result from chemotherapy, as ANLL has been linked to alkylating agents used for several cancers (*42*), including the breast (*18*).

The increased risks of certain digestive cancers that appeared in later follow-up periods in the women treated with and without radiation also deserve attention. Whereas the evidence is not firm, surveys of multiple primaries have indicated associations between breast and colon cancers (*2, 5, 8*). Strong positive correlations between incidence (and mortality) rates for these tumors have also been seen (*43, 44*). The nature of the relationship is unclear, although dietary and hormonal etiologies have been suggested (*45, 46*). The constellation of tumors appears also to encompass ovarian and uterine corpus cancers, both of which have been linked to colon and breast cancers (*29*). Genetic factors may also be involved in view of the tendency of these tumors to segregate in certain high-risk families (*47*).

Other cancer excesses are less readily explained. For example, it is unclear why women irradiated for breast cancer might be at higher risk for renal cancer and non-Hodgkin's lymphoma. Also unexplained is why breast cancer patients might be at decreased risk of multiple myeloma and CLL. Similar to a previous report (*7*), cancer of the salivary glands was increased above expectation, although the excess risk did not reach the level of statistical significance. However, in many of these observations, the role of chance is possible because of the substantial number of multiple comparisons.

In summary, women who are diagnosed with breast cancer are at a significantly elevated risk of developing a second primary cancer, most likely of the opposite breast, which exhibits a threefold excess risk. This risk is higher among women less than 55 years of age at initial breast cancer diagnosis but only slightly higher in women who received radiotherapy. The elevated risks of ovarian and uterine corpus cancers, and to a lesser extent melanoma and thyroid neoplasms, suggest common etiologic factors of a hormonal nature. Radiotherapy may have effected the increase in risk of cancers of the lung, esophagus, and connective tissue, and possibly ANLL. However, the evidence is far from conclusive, when one considers some increases in risk among those not treated with radiation and the possible role of chemotherapy or other treatments. When second breast cancers are excluded from analysis, women over the age of 55 at diagnosis (i.e., nearly 60% of all women with breast cancers) were not at overall increased risk of developing a second cancer. Further study is clearly warranted if we are to evaluate the role of underlying environmental and host determinants plus treatment effects in the development of second primaries following breast cancer.

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TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the breast, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	—	41,109	41,109
No. who developed a second primary cancer	—	3,984	3,984
Average age at diagnosis of first cancer, yr	—	59	59
Average yr of diagnosis of first cancer	—	1964	1964
Person-yr of follow-up	—	271,524	271,524
Average follow-up, yr	—	6.6	6.6
Percent given radiotherapy for first cancer	—	28.4	28.4

[a] ICD-O code = 174. Male breast cancers are not included in this set of tables.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the breast in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	3,657	91.8
Only the first cancer	235	5.9
Only the second cancer	73	1.8
Neither first nor second cancer	19	0.5
Total second primary cancers	3,984	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

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TABLE 1C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	41,109			36,068			18,609			9,306			41,109		
Person-yr in interval	32,043			103,274			66,162			70,046			271,524		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**413**	**247.91**	**1.7[b]**	**1,412**	**842.22**	**1.7[b]**	**964**	**588.98**	**1.6[b]**	**1,195**	**747.99**	**1.6[b]**	**3,984**	**2,425.68**	**1.6[b]**
All excluding site of initial cancer	**172**	**181.10**	**0.9**	**658**	**616.35**	**1.1**	**497**	**433.32**	**1.1[b]**	**730**	**559.48**	**1.3[b]**	**2,057**	**1,789.22**	**1.1[b]**
Buccal cavity, pharynx	**5**	**4.35**	**1.1**	**23**	**14.97**	**1.5**	**9**	**10.62**	**0.8**	**19**	**13.39**	**1.4**	**56**	**43.30**	**1.3**
Lip	1	0.26	3.8	1	0.87	1.1	1	0.61	1.6	2	0.78	2.6	5	2.53	2.0
Tongue	1	0.88	1.1	8	3.05	2.6[b]	2	2.18	0.9	3	2.75	1.1	14	8.85	1.6
Salivary gland	0	0.56	0.0	4	1.89	2.1	1	1.31	0.8	5	1.59	3.1[b]	10	5.34	1.9
Gum, other mouth	2	1.50	1.3	8	5.19	1.5	4	3.70	1.1	4	4.79	0.8	18	15.17	1.2
Pharynx	1	0.97	1.0	2	3.35	0.6	1	2.38	0.4	4	2.95	1.4	8	9.65	0.8
Digestive system	**74**	**73.29**	**1.0**	**263**	**249.98**	**1.1**	**194**	**177.27**	**1.1**	**297**	**235.80**	**1.3[b]**	**828**	**735.92**	**1.1[b]**
Esophagus	1	1.69	0.6	4	5.78	0.7	5	4.08	1.2	6	5.33	1.1	16	16.86	0.9
Stomach	12	9.98	1.2	39	32.99	1.2	29	22.52	1.3	22	27.43	0.8	102	92.86	1.1
Colon	27	33.89	0.8	114	116.68	1.0	104	83.76	1.2[b]	166	114.12	1.5[b]	411	348.26	1.2[b]
Rectum	23	14.03	1.6[b]	53	47.88	1.1	30	33.88	0.9	53	44.70	1.2	159	140.40	1.1
Liver, biliary	4	4.95	0.8	17	16.64	1.0	10	11.66	0.9	14	15.26	0.9	45	48.49	0.9
Pancreas	6	7.23	0.8	31	24.90	1.2	9	17.84	0.5[b]	31	24.64	1.3	77	74.56	1.0
Respiratory system	**7**	**14.91**	**0.5[b]**	**54**	**52.23**	**1.0**	**42**	**37.62**	**1.1**	**90**	**50.44**	**1.8[b]**	**193**	**155.10**	**1.2[b]**
Nasal cavities, sinuses	0	0.43	0.0	1	1.43	0.7	2	0.98	2.0	2	1.20	1.7	5	4.04	1.2
Larynx	1	0.90	1.1	3	3.13	1.0	2	2.25	0.9	3	2.81	1.1	9	9.08	1.0
Trachea, bronchus, lung	5	13.39	0.4[b]	50	47.03	1.1	37	33.95	1.1	85	45.86	1.9[b]	177	140.16	1.3[b]
Female breast	241	66.81	3.6[b]	754	225.87	3.3[b]	467	155.66	3.0[b]	465	188.51	2.5[b]	1,927	636.46	3.0[b]
Female genital tract	**52**	**42.46**	**1.2**	**176**	**141.16**	**1.2[b]**	**146**	**95.96**	**1.5[b]**	**161**	**112.01**	**1.4[b]**	**535**	**391.34**	**1.4[b]**
Cervix uteri	9	9.11	1.0	32	28.76	1.1	19	18.18	1.0	16	18.27	0.9	76	74.28	1.0
Corpus uteri	19	16.37	1.2	76	56.25	1.4[b]	65	39.88	1.6[b]	67	49.93	1.3[b]	227	162.34	1.4[b]
Uterus, NOS	1	3.23	0.3	7	10.02	0.7	4	6.21	0.6	10	5.76	1.7	22	25.20	0.9
Ovary, fallopian tubes	21	11.46	1.8[b]	52	38.42	1.4[b]	50	26.30	1.9[b]	60	31.02	1.9[b]	183	107.14	1.7[b]
Kidney, renal pelvis, ureter	5	3.74	1.3	16	12.88	1.2	9	9.11	1.0	6	12.05	0.5	36	37.75	1.0
Bladder, other urinary	5	6.58	0.8	29	22.85	1.3	15	16.46	0.9	24	22.64	1.1	73	68.50	1.1
Melanoma of the skin	5	3.02	1.7	18	10.29	1.8[b]	8	7.04	1.1	12	8.23	1.5	43	28.56	1.5[b]
Eye	0	0.42	0.0	6	1.41	4.2[b]	0	0.97	0.0	4	1.22	3.3	10	4.02	2.5[b]
Brain, central nervous system	2	2.51	0.8	7	8.56	0.8	3	5.95	0.5	9	7.33	1.2	21	24.34	0.9
Thyroid gland	6	1.91	3.1[b]	7	6.31	1.1	8	4.18	1.9	7	4.76	1.5	28	17.15	1.6[b]
Bone	1	0.39	2.6	1	1.25	0.8	0	0.81	0.0	2	0.90	2.2	4	3.35	1.2
Connective tissue	0	1.07	0.0	9	3.58	2.5[b]	7	2.44	2.9[b]	7	2.98	2.3	23	10.07	2.3[b]
Lymphatic, hematopoietic system	**8**	**15.22**	**0.5**	**34**	**52.45**	**0.6[b]**	**39**	**37.51**	**1.0**	**56**	**51.24**	**1.1**	**137**	**156.33**	**0.9**
Non-Hodgkin's lymphoma	5	5.77	0.9	15	19.99	0.8	17	14.34	1.2	17	19.34	0.9	54	59.40	0.9
Hodgkin's disease	0	1.17	0.0	3	3.81	0.8	2	2.57	0.8	3	3.10	1.0	8	10.64	0.8
Multiple myeloma	2	2.54	0.8	3	8.92	0.3[b]	3	6.54	0.5	6	9.55	0.6	14	27.53	0.5[b]
Leukemias	1	5.71	0.2[b]	13	19.63	0.7	17	14.02	1.2	30	19.20	1.6[b]	61	58.53	1.0
Chronic lymphocytic	0	1.55	0.0	1	5.43	0.2	2	3.95	0.5	6	5.79	1.0	9	16.72	0.5
Acute nonlymphocytic	1	1.89	0.5	7	6.56	1.1	10	4.73	2.1[b]	11	6.66	1.7	29	19.83	1.5

[a] ICD-O code = 174.
[b] $P < .05$.

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TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	11,691			9,750			4,366			2,002			11,691		
Person-yr in interval	8,865			25,846			15,102			13,283			63,096		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**129**	**61.98**	**2.1**[b]	**407**	**193.78**	**2.1**[b]	**245**	**126.57**	**1.9**[b]	**259**	**132.41**	**2.0**[b]	**1,040**	**514.41**	**2.0**[b]
All excluding site of initial cancer	**48**	**44.56**	**1.1**	**154**	**139.55**	**1.1**	**131**	**91.91**	**1.4**[b]	**163**	**98.21**	**1.7**[b]	**496**	**374.00**	**1.3**[b]
Buccal cavity, pharynx	**2**	**1.12**	**1.8**	**4**	**3.58**	**1.1**	**2**	**2.39**	**0.8**	**4**	**2.45**	**1.6**	**12**	**9.53**	**1.3**
Lip	0	0.06	0.0	0	0.18	0.0	0	0.12	0.0	1	0.13	7.6	1	0.50	2.0
Tongue	0	0.23	0.0	0	0.74	0.0	1	0.48	2.1	2	0.51	4.0	3	1.95	1.5
Salivary gland	0	0.14	0.0	1	0.44	2.3	0	0.28	0.0	0	0.28	0.0	1	1.14	0.9
Gum, other mouth	2	0.38	5.3	2	1.23	1.6	1	0.84	1.2	0	0.86	0.0	5	3.30	1.5
Pharynx	0	0.26	0.0	1	0.84	1.2	0	0.56	0.0	0	0.57	0.0	1	2.23	0.4
Digestive system	**14**	**17.07**	**0.8**	**56**	**53.35**	**1.0**	**54**	**35.41**	**1.5**[b]	**54**	**39.81**	**1.4**[b]	**178**	**145.55**	**1.2**[b]
Esophagus	1	0.41	2.5	0	1.30	0.0	3	0.88	3.4	2	0.93	2.2	6	3.51	1.7
Stomach	4	2.24	1.8	10	6.66	1.5	8	4.20	1.9	4	4.56	0.9	26	17.65	1.5
Colon	3	7.87	0.4	22	24.92	0.9	27	16.77	1.6[b]	28	19.17	1.5	80	68.68	1.2
Rectum	6	3.37	1.8	15	10.55	1.4	11	6.98	1.6	7	7.72	0.9	39	28.61	1.4
Liver, biliary	0	1.12	0.0	4	3.42	1.2	2	2.23	0.9	2	2.55	0.8	8	9.32	0.9
Pancreas	0	1.69	0.0	5	5.41	0.9	1	3.64	0.3	8	4.14	1.9	14	14.87	0.9
Respiratory system	**2**	**3.86**	**0.5**	**9**	**12.94**	**0.7**	**10**	**9.14**	**1.1**	**26**	**9.44**	**2.8**[b]	**47**	**35.36**	**1.3**
Nasal cavities, sinuses	0	0.11	0.0	0	0.33	0.0	0	0.21	0.0	1	0.22	4.6	1	0.87	1.1
Larynx	0	0.24	0.0	1	0.79	1.3	1	0.55	1.8	1	0.55	1.8	3	2.13	1.4
Trachea, bronchus, lung	2	3.46	0.6	8	11.66	0.7	9	8.28	1.1	24	8.57	2.8[b]	43	31.94	1.3
Female breast	81	17.42	4.7[b]	253	54.23	4.7[b]	114	34.66	3.3[b]	96	34.20	2.8[b]	544	140.41	3.9[b]
Female genital tract	**18**	**11.29**	**1.6**	**49**	**34.10**	**1.4**[b]	**33**	**21.36**	**1.5**[b]	**37**	**20.92**	**1.8**[b]	**137**	**87.61**	**1.6**[b]
Cervix uteri	0	2.49	0.0	6	6.98	0.9	3	3.98	0.8	5	3.49	1.4	14	16.93	0.8
Corpus uteri	6	4.43	1.4	25	14.09	1.8[b]	15	9.29	1.6	13	9.42	1.4	59	37.21	1.6[b]
Uterus, NOS	1	0.78	1.3	1	2.08	0.5	1	1.17	0.9	2	1.05	1.9	5	5.07	1.0
Ovary, fallopian tubes	11	3.05	3.6[b]	12	9.29	1.3	13	5.85	2.2[b]	14	5.77	2.4[b]	50	23.94	2.1[b]
Kidney, renal pelvis, ureter	3	0.93	3.2	7	2.95	2.4	3	1.97	1.5	2	2.14	0.9	15	7.98	1.9[b]
Bladder, other urinary	1	1.52	0.7	4	4.93	0.8	3	3.37	0.9	3	3.81	0.8	11	13.63	0.8
Melanoma of the skin	1	0.80	1.2	6	2.56	2.3	0	1.66	0.0	3	1.54	1.9	10	6.57	1.5
Eye	0	0.11	0.0	2	0.32	6.2	0	0.20	0.0	1	0.21	4.7	3	0.85	3.5
Brain, central nervous system	2	0.69	2.9	1	2.14	0.5	0	1.38	0.0	1	1.40	0.7	4	5.61	0.7
Thyroid gland	1	0.51	2.0	0	1.53	0.0	2	0.93	2.2	3	0.86	3.5	6	3.83	1.6
Bone	0	0.10	0.0	1	0.28	3.5	0	0.17	0.0	1	0.16	6.1	2	0.71	2.8
Connective tissue	0	0.27	0.0	2	0.82	2.4	3	0.51	5.8[b]	4	0.53	7.6[b]	9	2.12	4.2[b]
Lymphatic, hematopoietic system	**3**	**3.70**	**0.8**	**9**	**11.83**	**0.8**	**13**	**7.95**	**1.6**	**18**	**8.80**	**2.0**[b]	**43**	**32.26**	**1.3**
Non-Hodgkin's lymphoma	2	1.42	1.4	4	4.59	0.9	7	3.15	2.2	8	3.42	2.3[b]	21	12.58	1.7[b]
Hodgkin's disease	0	0.32	0.0	0	0.92	0.0	0	0.55	0.0	1	0.56	1.8	1	2.35	0.4
Multiple myeloma	0	0.62	0.0	0	2.05	0.0	0	1.41	0.0	2	1.62	1.2	2	5.70	0.4
Leukemias	1	1.34	0.7	5	4.25	1.2	6	2.82	2.1	7	3.18	2.2	19	11.59	1.6
Chronic lymphocytic	0	0.36	0.0	0	1.17	0.0	2	0.80	2.5	2	0.95	2.1	4	3.27	1.2
Acute nonlymphocytic	1	0.45	2.2	3	1.47	2.0	3	0.99	3.0	3	1.11	2.7	10	4.02	2.5[b]

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[a] ICD-O code = 174.

[b] $P < .05$.

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TABLE 1E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females not given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	29,418			26,318			14,243			7,304			29,418		
Person-yr in interval	23,177			77,428			51,060			56,763			208,428		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**284**	**185.93**	**1.5**[b]	**1,005**	**648.43**	**1.5**[b]	**719**	**462.41**	**1.6**[b]	**936**	**615.59**	**1.5**[b]	**2,944**	**1,911.27**	**1.5**[b]
All excluding site of initial cancer	**124**	**136.53**	**0.9**	**504**	**476.79**	**1.1**	**366**	**341.41**	**1.1**	**567**	**461.28**	**1.2**[b]	**1,561**	**1,415.22**	**1.1**[b]
Buccal cavity, pharynx	**3**	**3.23**	**0.9**	**19**	**11.39**	**1.7**[b]	**7**	**8.23**	**0.9**	**15**	**10.94**	**1.4**	**44**	**33.77**	**1.3**
Lip	1	0.20	5.0	1	0.69	1.5	1	0.49	2.0	1	0.65	1.5	4	2.03	2.0
Tongue	1	0.65	1.5	8	2.31	3.5[b]	1	1.69	0.6	1	2.25	0.4	11	6.90	1.6
Salivary gland	0	0.42	0.0	3	1.45	2.1	1	1.03	1.0	5	1.31	3.8[b]	9	4.21	2.1
Gum, other mouth	0	1.12	0.0	6	3.96	1.5	3	2.87	1.0	4	3.93	1.0	13	11.87	1.1
Pharynx	1	0.71	1.4	1	2.51	0.4	1	1.82	0.5	4	2.38	1.7	7	7.42	0.9
Digestive system	**60**	**56.22**	**1.1**	**207**	**196.63**	**1.1**	**140**	**141.86**	**1.0**	**243**	**195.99**	**1.2**[b]	**650**	**590.37**	**1.1**[b]
Esophagus	0	1.28	0.0	4	4.48	0.9	2	3.20	0.6	4	4.40	0.9	10	13.35	0.7
Stomach	8	7.74	1.0	29	26.33	1.1	21	18.32	1.1	18	22.87	0.8	76	75.21	1.0
Colon	24	26.02	0.9	92	91.76	1.0	77	66.99	1.1	138	94.96	1.5[b]	331	279.58	1.2[b]
Rectum	17	10.66	1.6	38	37.33	1.0	19	26.90	0.7	46	36.97	1.2	120	111.80	1.1
Liver, biliary	4	3.83	1.0	13	13.22	1.0	8	9.44	0.8	12	12.71	0.9	37	39.17	0.9
Pancreas	6	5.53	1.1	26	19.50	1.3	8	14.20	0.6	23	20.50	1.1	63	59.69	1.1
Respiratory system	**5**	**11.04**	**0.5**	**45**	**39.28**	**1.1**	**32**	**28.48**	**1.1**	**64**	**41.00**	**1.6**[b]	**146**	**119.74**	**1.2**[b]
Nasal cavities, sinuses	0	0.32	0.0	1	1.09	0.9	2	0.77	2.6	1	0.99	1.0	4	3.16	1.3
Larynx	1	0.66	1.5	2	2.34	0.9	1	1.70	0.6	2	2.27	0.9	6	6.95	0.9
Trachea, bronchus, lung	3	9.93	0.3[b]	42	35.38	1.2	28	25.67	1.1	61	37.29	1.6[b]	134	108.21	1.2[b]
Female breast	160	49.40	3.2[b]	501	171.64	2.9[b]	353	121.00	2.9[b]	369	154.31	2.4[b]	1,383	496.05	2.8[b]
Female genital tract	**34**	**31.17**	**1.1**	**127**	**107.06**	**1.2**	**113**	**74.59**	**1.5**[b]	**124**	**91.09**	**1.4**[b]	**398**	**303.73**	**1.3**[b]
Cervix uteri	9	6.62	1.4	26	21.78	1.2	16	14.20	1.1	11	14.78	0.7	62	57.35	1.1
Corpus uteri	13	11.94	1.1	51	42.17	1.2	50	30.59	1.6[b]	54	40.51	1.3[b]	168	125.13	1.3[b]
Uterus, NOS	0	2.46	0.0	6	7.93	0.8	3	5.04	0.6	8	4.71	1.7	17	20.12	0.8
Ovary, fallopian tubes	10	8.41	1.2	40	29.13	1.4	37	20.46	1.8[b]	46	25.25	1.8[b]	133	83.19	1.6[b]
Kidney, renal pelvis, ureter	2	2.81	0.7	9	9.92	0.9	6	7.14	0.8	4	9.90	0.4	21	29.77	0.7
Bladder, other urinary	4	5.06	0.8	25	17.91	1.4	12	13.09	0.9	21	18.84	1.1	62	54.87	1.1
Melanoma of the skin	4	2.22	1.8	12	7.72	1.6	8	5.37	1.5	9	6.69	1.3	33	21.99	1.5[b]
Eye	0	0.32	0.0	4	1.09	3.7	0	0.77	0.0	3	1.00	3.0	7	3.17	2.2
Brain, central nervous system	0	1.83	0.0	6	6.42	0.9	3	4.57	0.7	8	5.93	1.3	17	18.73	0.9
Thyroid gland	5	1.40	3.6[b]	7	4.78	1.5	6	3.26	1.8	4	3.89	1.0	22	13.32	1.7[b]
Bone	1	0.29	3.4	0	0.97	0.0	0	0.64	0.0	1	0.74	1.4	2	2.64	0.8
Connective tissue	0	0.80	0.0	7	2.76	2.5[b]	4	1.93	2.1	3	2.46	1.2	14	7.94	1.8
Lymphatic, hematopoietic system	**5**	**11.52**	**0.4**	**25**	**40.62**	**0.6**[b]	**26**	**29.56**	**0.9**	**38**	**42.43**	**0.9**	**94**	**124.06**	**0.8**[b]
Non-Hodgkin's lymphoma	3	4.35	0.7	11	15.40	0.7	10	11.18	0.9	9	15.92	0.6	33	46.82	0.7[b]
Hodgkin's disease	0	0.85	0.0	3	2.89	1.0	2	2.02	1.0	2	2.53	0.8	7	8.29	0.8
Multiple myeloma	2	1.92	1.0	3	6.86	0.4	3	5.13	0.6	4	7.93	0.5	12	21.83	0.5[b]
Leukemias	0	4.37	0.0[b]	8	15.38	0.5	11	11.20	1.0	23	16.02	1.4	42	46.94	0.9
Chronic lymphocytic	0	1.19	0.0	1	4.25	0.2	0	3.16	0.0	4	4.85	0.8	5	13.44	0.4[b]
Acute nonlymphocytic	0	1.44	0.0	4	5.10	0.8	7	3.74	1.9	8	5.55	1.4	19	15.81	1.2

[a] ICD-O code = 174.

[b] $P < .05$.

BREAST
FEMALES
AGES <45 YR

TABLE 1F.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females, aged <45 yr in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval		6,958			6,287			3,679			2,329			6,958	
Person-yr in interval		5,522			18,964			14,563			23,640			62,688	
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**69**	**10.10**	**6.8**[b]	**245**	**47.03**	**5.2**[b]	**158**	**52.54**	**3.0**[b]	**327**	**167.78**	**1.9**[b]	**799**	**277.36**	**2.9**[b]
All excluding site of initial cancer	**8**	**5.91**	**1.4**	**51**	**27.21**	**1.9**[b]	**45**	**31.60**	**1.4**[b]	**177**	**117.28**	**1.5**[b]	**281**	**181.94**	**1.5**[b]
Buccal cavity, pharynx	**1**	**0.13**	**7.9**	**2**	**0.72**	**2.8**	**1**	**0.98**	**1.0**	**6**	**3.56**	**1.7**	**10**	**5.39**	**1.9**
Lip	0	0.01	0.0	0	0.02	0.0	0	0.03	0.0	1	0.13	7.7	1	0.19	5.4
Tongue	0	0.02	0.0	0	0.15	0.0	0	0.19	0.0	2	0.74	2.7	2	1.09	1.8
Salivary gland	0	0.03	0.0	1	0.15	6.8	0	0.15	0.0	2	0.36	5.6	3	0.68	4.4
Gum, other mouth	1	0.03	31.6	1	0.22	4.6	1	0.33	3.1	1	1.21	0.8	4	1.79	2.2
Pharynx	0	0.03	0.0	0	0.16	0.0	0	0.24	0.0	0	0.95	0.0	0	1.37	0.0
Digestive system	**0**	**1.03**	**0.0**	**16**	**5.37**	**3.0**[b]	**6**	**7.31**	**0.8**	**64**	**38.41**	**1.7**[b]	**86**	**52.11**	**1.7**[b]
Esophagus	0	0.01	0.0	0	0.14	0.0	0	0.23	0.0	2	1.13	1.8	2	1.51	1.3
Stomach	0	0.14	0.0	0	0.65	0.0	2	0.80	2.5	4	3.66	1.1	6	5.24	1.1
Colon	0	0.49	0.0	7	2.54	2.8[b]	2	3.38	0.6	30	18.26	1.6[b]	39	24.66	1.6[b]
Rectum	0	0.25	0.0	4	1.24	3.2	1	1.74	0.6	17	8.41	2.0[b]	22	11.64	1.9[b]
Liver, biliary	0	0.05	0.0	2	0.23	8.7	0	0.33	0.0	2	2.11	0.9	4	2.72	1.5
Pancreas	0	0.05	0.0	3	0.36	8.3[b]	0	0.60	0.0	6	4.04	1.5	9	5.06	1.8
Respiratory system	**0**	**0.41**	**0.0**	**3**	**2.23**	**1.3**	**4**	**3.02**	**1.3**	**24**	**13.65**	**1.8**[b]	**31**	**19.31**	**1.6**[b]
Nasal cavities, sinuses	0	0.02	0.0	0	0.08	0.0	0	0.10	0.0	0	0.30	0.0	0	0.49	0.0
Larynx	0	0.04	0.0	0	0.18	0.0	0	0.25	0.0	1	0.93	1.1	1	1.39	0.7
Trachea, bronchus, lung	0	0.35	0.0	3	1.93	1.6	3	2.64	1.1	23	12.26	1.9[b]	29	17.19	1.7[b]
Female breast	61	4.19	14.6[b]	194	19.82	9.8[b]	113	20.94	5.4[b]	150	50.50	3.0[b]	518	95.42	5.4[b]
Female genital tract	**3**	**2.47**	**1.2**	**20**	**11.01**	**1.8**[b]	**21**	**11.99**	**1.8**[b]	**47**	**32.34**	**1.5**[b]	**91**	**57.79**	**1.6**[b]
Cervix uteri	1	1.16	0.9	6	4.31	1.4	6	3.61	1.7	6	6.06	1.0	19	15.13	1.3
Corpus uteri	0	0.44	0.0	0	2.62	0.0	6	3.94	1.5	19	15.13	1.3	25	22.13	1.1
Uterus, NOS	0	0.12	0.0	1	0.58	1.7	1	0.63	1.6	1	1.15	0.9	3	2.47	1.2
Ovary, fallopian tubes	2	0.68	2.9	12	3.18	3.8[b]	8	3.49	2.3	20	8.83	2.3[b]	42	16.18	2.6[b]
Kidney, renal pelvis, ureter	0	0.10	0.0	0	0.50	0.0	1	0.61	1.6	1	2.55	0.4	2	3.76	0.5
Bladder, other urinary	0	0.09	0.0	0	0.51	0.0	0	0.70	0.0	3	3.77	0.8	3	5.07	0.6
Melanoma of the skin	1	0.35	2.9	2	1.35	1.5	0	1.27	0.0	7	2.54	2.8[b]	10	5.50	1.8
Eye	0	0.01	0.0	0	0.07	0.0	0	0.09	0.0	2	0.27	7.3	2	0.45	4.4
Brain, central nervous system	0	0.17	0.0	1	0.71	1.4	0	0.76	0.0	3	2.29	1.3	4	3.92	1.0
Thyroid gland	2	0.27	7.4	2	1.00	2.0	5	0.79	6.4[b]	2	1.35	1.5	11	3.40	3.2[b]
Bone	0	0.02	0.0	0	0.09	0.0	0	0.08	0.0	1	0.19	5.2	1	0.38	2.6
Connective tissue	0	0.08	0.0	1	0.31	3.3	1	0.28	3.6	0	0.70	0.0	2	1.37	1.5
Lymphatic, hematopoietic system	**0**	**0.56**	**0.0**	**3**	**2.29**	**1.3**	**5**	**2.39**	**2.1**	**9**	**9.72**	**0.9**	**17**	**14.96**	**1.1**
Non-Hodgkin's lymphoma	0	0.21	0.0	1	0.91	1.1	2	1.00	2.0	4	4.13	1.0	7	6.24	1.1
Hodgkin's disease	0	0.14	0.0	0	0.46	0.0	0	0.35	0.0	0	0.81	0.0	0	1.75	0.0
Multiple myeloma	0	0.03	0.0	0	0.16	0.0	0	0.25	0.0	3	1.73	1.7	3	2.17	1.4
Leukemias	0	0.18	0.0	2	0.77	2.6	3	0.80	3.8	2	3.05	0.7	7	4.80	1.5
Chronic lymphocytic	0	0.01	0.0	0	0.09	0.0	0	0.12	0.0	0	0.83	0.0	0	1.07	0.0
Acute nonlymphocytic	0	0.09	0.0	1	0.34	2.9	2	0.31	6.4	1	1.17	0.9	4	1.91	2.1

[a] ICD-O code = 174.

[b] $P < .05$.

BREAST
FEMALES
AGES 45–54 YR

TABLE 1G.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females, aged 45–54 yr in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	9,961			9,019			5,222			2,922			9,961		
Person-yr in interval	7,923			27,183			19,624			23,828			78,557		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**97**	**35.18**	**2.8**[b]	**334**	**139.27**	**2.4**[b]	**250**	**127.71**	**2.0**[b]	**399**	**242.57**	**1.6**[b]	**1,080**	**544.48**	**2.0**[b]
All excluding site of initial cancer	**29**	**22.04**	**1.3**	**123**	**90.95**	**1.4**[b]	**117**	**88.40**	**1.3**[b]	**251**	**180.07**	**1.4**[b]	**520**	**381.30**	**1.4**[b]
Buccal cavity, pharynx	**0**	**0.69**	**0.0**	**2**	**2.91**	**0.7**	**3**	**2.84**	**1.1**	**5**	**4.69**	**1.1**	**10**	**11.13**	**0.9**
Lip	0	0.02	0.0	0	0.10	0.0	0	0.11	0.0	0	0.21	0.0	0	0.45	0.0
Tongue	0	0.12	0.0	0	0.56	0.0	1	0.58	1.7	1	1.00	1.0	2	2.26	0.9
Salivary gland	0	0.09	0.0	0	0.34	0.0	0	0.27	0.0	2	0.50	4.0	2	1.20	1.7
Gum, other mouth	0	0.24	0.0	2	0.96	2.1	1	0.92	1.1	1	1.63	0.6	4	3.74	1.1
Pharynx	0	0.18	0.0	0	0.78	0.0	1	0.79	1.3	1	1.17	0.9	2	2.92	0.7
Digestive system	**8**	**5.65**	**1.4**	**29**	**24.90**	**1.2**	**38**	**26.83**	**1.4**[b]	**82**	**69.91**	**1.2**	**157**	**127.25**	**1.2**[b]
Esophagus	0	0.18	0.0	2	0.82	2.4	0	0.87	0.0	2	1.69	1.2	4	3.56	1.1
Stomach	0	0.66	0.0	4	2.75	1.5	5	2.80	1.8	5	7.26	0.7	14	13.47	1.0
Colon	3	2.53	1.2	10	11.18	0.9	22	12.14	1.8[b]	40	33.61	1.2	75	59.43	1.3
Rectum	5	1.37	3.7[b]	2	5.95	0.3	6	6.25	1.0	18	14.20	1.3	31	27.76	1.1
Liver, biliary	0	0.29	0.0	4	1.29	3.1	3	1.46	2.1	6	4.36	1.4	13	7.39	1.8
Pancreas	0	0.48	0.0	5	2.27	2.2	0	2.67	0.0	10	7.51	1.3	15	12.92	1.2
Respiratory system	**2**	**2.12**	**0.9**	**9**	**9.51**	**0.9**	**14**	**9.96**	**1.4**	**43**	**18.93**	**2.3**[b]	**68**	**40.49**	**1.7**[b]
Nasal cavities, sinuses	0	0.07	0.0	1	0.27	3.7	1	0.23	4.3	1	0.40	2.5	3	0.98	3.1
Larynx	0	0.17	0.0	0	0.79	0.0	1	0.78	1.3	2	1.08	1.9	3	2.82	1.1
Trachea, bronchus, lung	2	1.85	1.1	8	8.32	1.0	12	8.82	1.4	40	17.24	2.3[b]	62	36.22	1.7[b]
Female breast	68	13.14	5.2[b]	211	48.32	4.4[b]	133	39.31	3.4[b]	148	62.50	2.4[b]	560	163.18	3.4[b]
Female genital tract	**16**	**8.22**	**1.9**[b]	**50**	**31.79**	**1.6**[b]	**33**	**27.86**	**1.2**	**60**	**40.37**	**1.5**[b]	**159**	**108.20**	**1.5**[b]
Cervix uteri	1	2.24	0.4	9	7.65	1.2	7	5.69	1.2	5	6.44	0.8	22	22.00	1.0
Corpus uteri	5	2.93	1.7	20	12.87	1.6	9	12.76	0.7	27	19.19	1.4	61	47.73	1.3
Uterus, NOS	0	0.51	0.0	1	1.77	0.6	0	1.35	0.0	2	1.64	1.2	3	5.26	0.6
Ovary, fallopian tubes	10	2.32	4.3[b]	19	8.67	2.2[b]	17	7.30	2.3[b]	24	11.04	2.2[b]	70	29.31	2.4[b]
Kidney, renal pelvis, ureter	0	0.42	0.0	3	1.81	1.7	2	1.82	1.1	1	4.08	0.2	6	8.12	0.7
Bladder, other urinary	1	0.51	2.0	4	2.27	1.8	2	2.47	0.8	7	6.59	1.1	14	11.83	1.2
Melanoma of the skin	1	0.73	1.4	9	2.65	3.4[b]	5	1.95	2.6	3	2.72	1.1	18	8.04	2.2[b]
Eye	0	0.07	0.0	2	0.24	8.5	0	0.20	0.0	1	0.42	2.4	3	0.93	3.2
Brain, central nervous system	0	0.49	0.0	3	1.99	1.5	2	1.84	1.1	4	2.90	1.4	9	7.23	1.2
Thyroid gland	1	0.39	2.5	3	1.38	2.2	2	1.04	1.9	5	1.49	3.3[b]	11	4.31	2.6[b]
Bone	0	0.06	0.0	1	0.19	5.4	0	0.14	0.0	1	0.31	3.2	2	0.70	2.9
Connective tissue	0	0.17	0.0	1	0.67	1.5	5	0.58	8.7[b]	5	0.91	5.5[b]	11	2.33	4.7[b]
Lymphatic, hematopoietic system	**0**	**1.55**	**0.0**	**6**	**6.50**	**0.9**	**8**	**6.67**	**1.2**	**23**	**16.24**	**1.4**	**37**	**30.95**	**1.2**
Non-Hodgkin's lymphoma	0	0.64	0.0	3	2.79	1.1	4	2.94	1.4	7	6.46	1.1	14	12.82	1.1
Hodgkin's disease	0	0.19	0.0	1	0.71	1.4	2	0.61	3.3	2	1.10	1.8	5	2.61	1.9
Multiple myeloma	0	0.19	0.0	0	0.91	0.0	0	1.08	0.0	2	3.11	0.6	2	5.28	0.4
Leukemias	0	0.53	0.0	2	2.10	1.0	2	2.03	1.0	12	5.53	2.2[b]	16	10.18	1.6
Chronic lymphocytic	0	0.09	0.0	0	0.39	0.0	0	0.46	0.0	3	1.71	1.8	3	2.65	1.1
Acute nonlymphocytic	0	0.18	0.0	0	0.77	0.0	1	0.78	1.3	3	1.98	1.5	4	3.70	1.1

[a] ICD-O code = 174.

[b] $P < .05$.

BREAST
FEMALES
AGES 55+ YR

TABLE 1H.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females, aged 55+ yr in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	24,190			20,762			9,708			4,055			24,190		
Person-yr in interval	18,599			57,127			31,975			22,578			130,278		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**247**	**202.63**	**1.2^{b}**	**833**	**655.91**	**1.3^{b}**	**556**	**408.73**	**1.4^{b}**	**469**	**337.65**	**1.4^{b}**	**2,105**	**1,603.83**	**1.3^{b}**
All excluding site of initial cancer	**135**	**153.15**	**0.9**	**484**	**498.18**	**1.0**	**335**	**313.32**	**1.1**	**302**	**262.15**	**1.2^{b}**	**1,256**	**1,225.97**	**1.0**
Buccal cavity, pharynx	**4**	**3.54**	**1.1**	**19**	**11.33**	**1.7^{b}**	**5**	**6.80**	**0.7**	**8**	**5.13**	**1.6**	**36**	**26.78**	**1.3**
Lip	1	0.23	4.3	1	0.74	1.3	1	0.47	2.1	1	0.44	2.3	4	1.89	2.1
Tongue	1	0.74	1.4	8	2.34	3.4^{b}	1	1.41	0.7	0	1.02	0.0	10	5.50	1.8
Salivary gland	0	0.43	0.0	3	1.40	2.1	1	0.89	1.1	1	0.74	1.4	5	3.46	1.4
Gum, other mouth	1	1.23	0.8	5	4.00	1.2	2	2.46	0.8	2	1.95	1.0	10	9.64	1.0
Pharynx	1	0.77	1.3	2	2.42	0.8	0	1.35	0.0	3	0.84	3.6	6	5.36	1.1
Digestive system	**66**	**66.60**	**1.0**	**218**	**219.71**	**1.0**	**150**	**143.12**	**1.0**	**151**	**127.49**	**1.2^{b}**	**585**	**556.56**	**1.1**
Esophagus	1	1.49	0.7	2	4.82	0.4	5	2.98	1.7	2	2.51	0.8	10	11.79	0.8
Stomach	12	9.18	1.3	35	29.59	1.2	22	18.92	1.2	13	16.51	0.8	82	74.15	1.1
Colon	24	30.88	0.8	97	102.96	0.9	80	68.23	1.2	96	62.26	1.5^{b}	297	264.16	1.1^{b}
Rectum	18	12.41	1.4	47	40.68	1.2	23	25.89	0.9	18	22.09	0.8	106	101.01	1.0
Liver, biliary	4	4.62	0.9	11	15.13	0.7	7	9.88	0.7	6	8.79	0.7	28	38.38	0.7
Pancreas	6	6.70	0.9	23	22.27	1.0	9	14.56	0.6	15	13.09	1.1	53	56.58	0.9
Respiratory system	**5**	**12.37**	**0.4^{b}**	**42**	**40.49**	**1.0**	**24**	**24.64**	**1.0**	**23**	**17.86**	**1.3**	**94**	**95.29**	**1.0**
Nasal cavities, sinuses	0	0.34	0.0	0	1.08	0.0	1	0.65	1.5	1	0.51	2.0	2	2.57	0.8
Larynx	1	0.69	1.5	3	2.16	1.4	1	1.22	0.8	0	0.80	0.0	5	4.86	1.0
Trachea, bronchus, lung	3	11.19	0.3^{b}	39	36.78	1.1	22	22.49	1.0	22	16.35	1.3	86	86.75	1.0
Female breast	112	49.48	2.3^{b}	349	157.73	2.2^{b}	221	95.41	2.3^{b}	167	75.50	2.2^{b}	849	377.86	2.2^{b}
Female genital tract	**33**	**31.76**	**1.0**	**106**	**98.36**	**1.1**	**92**	**56.10**	**1.6^{b}**	**54**	**39.30**	**1.4^{b}**	**285**	**225.36**	**1.3^{b}**
Cervix uteri	7	5.72	1.2	17	16.79	1.0	6	8.89	0.7	5	5.78	0.9	35	37.14	0.9
Corpus uteri	14	13.00	1.1	56	40.76	1.4^{b}	50	23.17	2.2^{b}	21	15.60	1.3	141	92.48	1.5^{b}
Uterus, NOS	1	2.60	0.4	5	7.66	0.7	3	4.23	0.7	7	2.97	2.4	16	17.46	0.9
Ovary, fallopian tubes	9	8.46	1.1	21	26.57	0.8	25	15.52	1.6^{b}	16	11.15	1.4	71	61.65	1.2
Kidney, renal pelvis, ureter	5	3.23	1.5	13	10.57	1.2	6	6.69	0.9	4	5.41	0.7	28	25.88	1.1
Bladder, other urinary	4	5.98	0.7	25	20.07	1.2	13	13.29	1.0	14	12.29	1.1	56	51.59	1.1
Melanoma of the skin	3	1.95	1.5	7	6.29	1.1	3	3.81	0.8	2	2.97	0.7	15	15.01	1.0
Eye	0	0.34	0.0	4	1.10	3.6	0	0.68	0.0	1	0.53	1.9	5	2.65	1.9
Brain, central nervous system	2	1.85	1.1	3	5.85	0.5	1	3.35	0.3	2	2.14	0.9	8	13.19	0.6
Thyroid gland	3	1.24	2.4	2	3.93	0.5	1	2.36	0.4	0	1.92	0.0	6	9.44	0.6
Bone	1	0.31	3.2	0	0.98	0.0	0	0.59	0.0	0	0.40	0.0	1	2.27	0.4
Connective tissue	0	0.82	0.0	7	2.60	2.7^{b}	1	1.59	0.6	2	1.37	1.5	10	6.37	1.6
Lymphatic, hematopoietic system	**8**	**13.11**	**0.6**	**25**	**43.65**	**0.6^{b}**	**26**	**28.45**	**0.9**	**24**	**25.27**	**0.9**	**83**	**110.41**	**0.8^{b}**
Non-Hodgkin's lymphoma	5	4.92	1.0	11	16.29	0.7	11	10.40	1.1	6	8.75	0.7	33	40.33	0.8
Hodgkin's disease	0	0.84	0.0	2	2.65	0.8	0	1.60	0.0	1	1.19	0.8	3	6.28	0.5
Multiple myeloma	2	2.32	0.9	3	7.84	0.4	3	5.21	0.6	1	4.71	0.2	9	20.08	0.4^{b}
Leukemias	1	5.00	0.2	9	16.76	0.5	12	11.20	1.1	16	10.62	1.5	38	43.56	0.9
Chronic lymphocytic	0	1.45	0.0	1	4.95	0.2	2	3.37	0.6	3	3.25	0.9	6	13.00	0.5
Acute nonlymphocytic	1	1.62	0.6	6	5.46	1.1	7	3.64	1.9	7	3.51	2.0	21	14.21	1.5

[a] ICD-O code = 174.
[b] $P < .05$.

BREAST
FEMALES
LONG-TERM SURVIVORS

TABLE 11.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	36,068			9,306			2,661			610			41,109		
Person-yr in interval	169,435			52,886			14,203			2,956			271,524		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2,376**	**1,430.76**	**1.7**[b]	**855**	**529.89**	**1.6**[b]	**280**	**173.18**	**1.6**[b]	**60**	**45.02**	**1.3**[b]	**3,984**	**2,425.68**	**1.6**[b]
All excluding site of initial cancer	**1,155**	**1,049.35**	**1.1**[b]	**505**	**394.00**	**1.3**[b]	**180**	**130.88**	**1.4**[b]	**45**	**34.68**	**1.3**	**2,057**	**1,789.22**	**1.1**[b]
Buccal cavity, pharynx	**32**	**25.58**	**1.3**	**17**	**9.63**	**1.8**[b]	**2**	**3.05**	**0.7**	**0**	**0.71**	**0.0**	**56**	**43.30**	**1.3**
Lip	2	1.48	1.3	2	0.55	3.6	0	0.18	0.0	0	0.05	0.0	5	2.53	2.0
Tongue	10	5.22	1.9	3	1.98	1.5	0	0.63	0.0	0	0.14	0.0	14	8.85	1.6
Salivary gland	5	3.19	1.6	5	1.13	4.4[b]	0	0.37	0.0	0	0.09	0.0	10	5.34	1.9
Gum, other mouth	12	8.89	1.4	3	3.40	0.9	1	1.12	0.9	0	0.27	0.0	18	15.17	1.2
Pharynx	3	5.73	0.5	3	2.18	1.4	1	0.64	1.6	0	0.13	0.0	8	9.65	0.8
Digestive system	**457**	**427.12**	**1.1**	**196**	**163.52**	**1.2**[b]	**81**	**56.33**	**1.4**[b]	**20**	**15.99**	**1.3**	**828**	**735.92**	**1.1**[b]
Esophagus	9	9.86	0.9	4	3.74	1.1	1	1.25	0.8	1	0.34	3.0	16	16.86	0.9
Stomach	68	55.49	1.2	18	19.62	0.9	3	6.17	0.5	1	1.64	0.6	102	92.86	1.1
Colon	218	200.37	1.1	114	78.27	1.5[b]	46	27.73	1.7[b]	6	8.15	0.7	411	348.26	1.2[b]
Rectum	83	81.74	1.0	29	31.26	0.9	18	10.57	1.7[b]	6	2.87	2.1	159	140.40	1.1
Liver, biliary	27	28.30	1.0	8	10.67	0.7	5	3.60	1.4	1	0.99	1.0	45	48.49	0.9
Pancreas	40	42.73	0.9	21	16.86	1.2	5	6.03	0.8	5	1.75	2.9	77	74.56	1.0
Respiratory system	**96**	**89.82**	**1.1**	**58**	**35.15**	**1.6**[b]	**26**	**12.25**	**2.1**[b]	**6**	**3.04**	**2.0**	**193**	**155.10**	**1.2**[b]
Nasal cavities, sinuses	3	2.41	1.2	2	0.87	2.3	0	0.27	0.0	0	0.06	0.0	5	4.04	1.2
Larynx	5	5.37	0.9	3	2.04	1.5	0	0.63	0.0	0	0.14	0.0	9	9.08	1.0
Trachea, bronchus, lung	87	80.96	1.1	53	31.84	1.7[b]	26	11.21	2.3[b]	6	2.81	2.1	177	140.16	1.3[b]
Female breast	1,221	381.41	3.2[b]	350	135.89	2.6[b]	100	42.30	2.4[b]	15	10.34	1.5	1,927	636.46	3.0[b]
Female genital tract	**322**	**237.05**	**1.4**[b]	**119**	**82.90**	**1.4**[b]	**37**	**23.99**	**1.5**[b]	**5**	**5.14**	**1.0**	**535**	**391.34**	**1.4**[b]
Cervix uteri	51	46.92	1.1	12	14.18	0.8	4	3.46	1.2	0	0.64	0.0	76	74.28	1.0
Corpus uteri	141	96.10	1.5[b]	46	36.44	1.3	17	11.15	1.5	4	2.34	1.7	227	162.34	1.4[b]
Uterus, NOS	11	16.22	0.7	7	4.59	1.5	3	0.98	3.1	0	0.18	0.0	22	25.20	0.9
Ovary, fallopian tubes	102	64.70	1.6[b]	46	22.80	2.0[b]	13	6.71	1.9[b]	1	1.51	0.7	183	107.14	1.7[b]
Kidney, renal pelvis, ureter	25	21.98	1.1	3	8.43	0.4	2	2.89	0.7	1	0.73	1.4	36	37.75	1.0
Bladder, other urinary	44	39.30	1.1	21	15.47	1.4	1	5.53	0.2	2	1.65	1.2	73	68.50	1.1
Melanoma of the skin	26	17.32	1.5	7	5.95	1.2	3	1.85	1.6	2	0.43	4.6	43	28.56	1.5[b]
Eye	6	2.38	2.5	2	0.88	2.3	2	0.28	7.1	0	0.06	0.0	10	4.02	2.5[b]
Brain, central nervous system	10	14.50	0.7	8	5.34	1.5	0	1.65	0.0	1	0.35	2.9	21	24.34	0.9
Thyroid gland	15	10.49	1.4	5	3.52	1.4	2	1.02	2.0	0	0.22	0.0	28	17.15	1.6[b]
Bone	1	2.06	0.5	2	0.66	3.0	0	0.20	0.0	0	0.05	0.0	4	3.35	1.2
Connective tissue	16	6.02	2.7[b]	5	2.15	2.3	2	0.66	3.0	0	0.17	0.0	23	10.07	2.3[b]
Lymphatic, hematopoietic system	**73**	**89.93**	**0.8**	**38**	**35.17**	**1.1**	**14**	**12.49**	**1.1**	**4**	**3.58**	**1.1**	**137**	**156.33**	**0.9**
Non-Hodgkin's lymphoma	32	34.31	0.9	11	13.37	0.8	6	4.66	1.3	0	1.31	0.0	54	59.40	0.9
Hodgkin's disease	5	6.38	0.8	2	2.25	0.9	1	0.70	1.4	0	0.14	0.0	8	10.64	0.8
Multiple myeloma	6	15.45	0.4[b]	2	6.38	0.3	2	2.44	0.8	2	0.73	2.8	14	27.53	0.5[b]
Leukemias	30	33.64	0.9	23	13.12	1.8[b]	5	4.68	1.1	2	1.40	1.4	61	58.53	1.0
Chronic lymphocytic	3	9.38	0.3[b]	4	3.87	1.0	1	1.48	0.7	1	0.45	2.2	9	16.72	0.5
Acute nonlymphocytic	17	11.29	1.5	7	4.48	1.6	4	1.66	2.4	0	0.52	0.0	29	19.83	1.5

[a] ICD-O code = 174.

[b] $P < .05$.

BREAST
FEMALES
LONG-TERM SURVIVORS
RADIOTHERAPY

TABLE 1J.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females given radiotherapy, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	9,750			2,002			455			96			11,691		
Person-yr in interval	40,947			10,224			2,520			540			63,096		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**652**	**320.26**	**2.0[b]**	**195**	**95.63**	**2.0[b]**	**56**	**28.83**	**1.9[b]**	**8**	**7.97**	**1.0**	**1,040**	**514.41**	**2.0[b]**
All excluding site of initial cancer	**285**	**231.40**	**1.2[b]**	**118**	**70.44**	**1.7[b]**	**40**	**21.67**	**1.8[b]**	**5**	**6.12**	**0.8**	**496**	**374.00**	**1.3[b]**
Buccal cavity, pharynx	**6**	**5.97**	**1.0**	**4**	**1.80**	**2.2**	**0**	**0.52**	**0.0**	**0**	**0.13**	**0.0**	**12**	**9.53**	**1.3**
Lip	0	0.30	0.0	1	0.09	10.6	0	0.03	0.0	0	0.01	0.0	1	0.50	2.0
Tongue	1	1.22	0.8	2	0.37	5.4	0	0.11	0.0	0	0.03	0.0	3	1.95	1.5
Salivary gland	1	0.71	1.4	0	0.20	0.0	0	0.06	0.0	0	0.02	0.0	1	1.14	0.9
Gum, other mouth	3	2.06	1.5	0	0.62	0.0	0	0.19	0.0	0	0.05	0.0	5	3.30	1.5
Pharynx	1	1.40	0.7	0	0.43	0.0	0	0.11	0.0	0	0.02	0.0	1	2.23	0.4
Digestive system	**110**	**88.73**	**1.2[b]**	**33**	**27.95**	**1.2**	**19**	**9.10**	**2.1[b]**	**2**	**2.77**	**0.7**	**178**	**145.55**	**1.2[b]**
Esophagus	3	2.18	1.4	2	0.66	3.0	0	0.21	0.0	0	0.06	0.0	6	3.51	1.7
Stomach	18	10.86	1.7	2	3.28	0.6	2	1.00	2.0	0	0.28	0.0	26	17.65	1.5
Colon	49	41.67	1.2	22	13.31	1.7[b]	6	4.44	1.3	0	1.41	0.0	80	68.68	1.2
Rectum	26	17.53	1.5	3	5.49	0.5	3	1.73	1.7	1	0.50	2.0	39	28.61	1.4
Liver, biliary	6	5.64	1.1	1	1.80	0.6	1	0.58	1.7	0	0.17	0.0	8	9.32	0.9
Pancreas	6	9.04	0.7	3	2.87	1.0	4	0.97	4.1[b]	1	0.31	3.3	14	14.87	0.9
Respiratory system	**19**	**22.08**	**0.9**	**16**	**6.81**	**2.4[b]**	**9**	**2.07**	**4.4[b]**	**1**	**0.57**	**1.8**	**47**	**35.36**	**1.3**
Nasal cavities, sinuses	0	0.54	0.0	1	0.16	6.2	0	0.05	0.0	0	0.01	0.0	1	0.87	1.1
Larynx	2	1.34	1.5	1	0.41	2.4	0	0.11	0.0	0	0.03	0.0	3	2.13	1.4
Trachea, bronchus, lung	17	19.93	0.9	14	6.16	2.3[b]	9	1.88	4.8[b]	1	0.52	1.9	43	31.94	1.3
Female breast	367	88.86	4.1[b]	77	25.19	3.1[b]	16	7.16	2.2[b]	3	1.85	1.6	544	140.41	3.9[b]
Female genital tract	**82**	**55.45**	**1.5[b]**	**31**	**15.75**	**2.0[b]**	**5**	**4.22**	**1.2**	**1**	**0.95**	**1.1**	**137**	**87.61**	**1.6[b]**
Cervix uteri	9	10.96	0.8	4	2.75	1.5	1	0.63	1.6	0	0.12	0.0	14	16.93	0.8
Corpus uteri	40	23.37	1.7[b]	10	7.02	1.4	2	1.97	1.0	1	0.44	2.3	59	37.21	1.6[b]
Uterus, NOS	2	3.25	0.6	2	0.85	2.4	0	0.17	0.0	0	0.03	0.0	5	5.07	1.0
Ovary, fallopian tubes	25	15.13	1.7[b]	12	4.31	2.8[b]	2	1.18	1.7	0	0.28	0.0	50	23.94	2.1[b]
Kidney, renal pelvis, ureter	10	4.92	2.0	1	1.52	0.7	0	0.49	0.0	1	0.13	7.4	15	7.98	1.9[b]
Bladder, other urinary	7	8.31	0.8	3	2.65	1.1	0	0.88	0.0	0	0.28	0.0	11	13.63	0.8
Melanoma of the skin	6	4.22	1.4	3	1.15	2.6	0	0.32	0.0	0	0.08	0.0	10	6.57	1.5
Eye	2	0.53	3.8	1	0.15	6.5	0	0.05	0.0	0	0.01	0.0	3	0.85	3.5
Brain, central nervous system	1	3.52	0.3	1	1.04	1.0	0	0.29	0.0	0	0.07	0.0	4	5.61	0.7
Thyroid gland	2	2.46	0.8	2	0.65	3.1	1	0.17	5.8	0	0.04	0.0	6	3.83	1.6
Bone	1	0.45	2.2	1	0.12	8.2	0	0.03	0.0	0	0.01	0.0	2	0.71	2.8
Connective tissue	5	1.33	3.8[b]	4	0.39	10.4[b]	0	0.11	0.0	0	0.03	0.0	9	2.12	4.2[b]
Lymphatic, hematopoietic system	**22**	**19.78**	**1.1**	**15**	**6.16**	**2.4[b]**	**3**	**2.02**	**1.5**	**0**	**0.63**	**0.0**	**43**	**32.26**	**1.3**
Non-Hodgkin's lymphoma	11	7.74	1.4	5	2.43	2.1	3	0.77	3.9	0	0.23	0.0	21	12.58	1.7[b]
Hodgkin's disease	0	1.47	0.0	1	0.41	2.4	0	0.12	0.0	0	0.03	0.0	1	2.35	0.4
Multiple myeloma	0	3.47	0.0	2	1.10	1.8	0	0.39	0.0	0	0.13	0.0	2	5.70	0.4
Leukemias	11	7.07	1.6	7	2.20	3.2[b]	0	0.74	0.0	0	0.24	0.0	19	11.59	1.6
Chronic lymphocytic	2	1.97	1.0	2	0.64	3.1	0	0.23	0.0	0	0.08	0.0	4	3.27	1.2
Acute nonlymphocytic	6	2.46	2.4	3	0.77	3.9	0	0.26	0.0	0	0.09	0.0	10	4.02	2.5[b]

[a] ICD-O code = 174.

[b] $P < .05$.

BREAST
FEMALES
LONG-TERM SURVIVORS
NO RADIOTHERAPY

TABLE 1K.– *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females not given radiotherapy, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	26,318			7,304			2,206			514			29,418		
Person-yr in interval	128,488			42,663			11,683			2,417			208,428		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1,724**	**1,110.51**	**1.6**[b]	**660**	**434.26**	**1.5**[b]	**224**	**144.36**	**1.6**[b]	**52**	**37.05**	**1.4**[b]	**2,944**	**1,911.27**	**1.5**[b]
All excluding site of initial cancer	**870**	**817.96**	**1.1**	**387**	**323.56**	**1.2**[b]	**140**	**109.22**	**1.3**[b]	**40**	**28.56**	**1.4**[b]	**1,561**	**1,415.22**	**1.1**[b]
Buccal cavity, pharynx	**26**	**19.61**	**1.3**	**13**	**7.83**	**1.7**	**2**	**2.53**	**0.8**	**0**	**0.58**	**0.0**	**44**	**33.77**	**1.3**
Lip	2	1.18	1.7	1	0.46	2.2	0	0.15	0.0	0	0.05	0.0	4	2.03	2.0
Tongue	9	4.00	2.2[b]	1	1.61	0.6	0	0.53	0.0	0	0.11	0.0	11	6.90	1.6
Salivary gland	4	2.48	1.6	5	0.93	5.4[b]	0	0.30	0.0	0	0.07	0.0	9	4.21	2.1
Gum, other mouth	9	6.82	1.3	3	2.78	1.1	1	0.93	1.1	0	0.23	0.0	13	11.87	1.1
Pharynx	2	4.33	0.5	3	1.75	1.7	1	0.53	1.9	0	0.11	0.0	7	7.42	0.9
Digestive system	**347**	**338.39**	**1.0**	**163**	**135.57**	**1.2**[b]	**62**	**47.23**	**1.3**[b]	**18**	**13.21**	**1.4**	**650**	**590.37**	**1.1**[b]
Esophagus	6	7.67	0.8	2	3.08	0.6	1	1.05	1.0	1	0.28	3.6	10	13.35	0.7
Stomach	50	44.63	1.1	16	16.34	1.0	1	5.17	0.2	1	1.36	0.7	76	75.21	1.0
Colon	169	158.70	1.1	92	64.96	1.4[b]	40	23.28	1.7[b]	6	6.73	0.9	331	279.58	1.2[b]
Rectum	57	64.21	0.9	26	25.77	1.0	15	8.84	1.7	5	2.37	2.1	120	111.80	1.1
Liver, biliary	21	22.65	0.9	7	8.87	0.8	4	3.01	1.3	1	0.82	1.2	37	39.17	0.9
Pancreas	34	33.68	1.0	18	13.99	1.3	1	5.06	0.2	4	1.45	2.8	63	59.69	1.1
Respiratory system	**77**	**67.74**	**1.1**	**42**	**28.35**	**1.5**[b]	**17**	**10.18**	**1.7**	**5**	**2.48**	**2.0**	**146**	**119.74**	**1.2**[b]
Nasal cavities, sinuses	3	1.86	1.6	1	0.71	1.4	0	0.23	0.0	0	0.05	0.0	4	3.16	1.3
Larynx	3	4.03	0.7	2	1.63	1.2	0	0.52	0.0	0	0.11	0.0	6	6.95	0.9
Trachea, bronchus, lung	70	61.03	1.1	39	25.68	1.5[b]	17	9.33	1.8[b]	5	2.29	2.2	134	108.21	1.2[b]
Female breast	854	292.55	2.9[b]	273	110.70	2.5[b]	84	35.14	2.4[b]	12	8.49	1.4	1,383	496.05	2.8[b]
Female genital tract	**240**	**181.60**	**1.3**[b]	**88**	**67.15**	**1.3**[b]	**32**	**19.77**	**1.6**[b]	**4**	**4.19**	**1.0**	**398**	**303.73**	**1.3**[b]
Cervix uteri	42	35.97	1.2	8	11.44	0.7	3	2.82	1.1	0	0.52	0.0	62	57.35	1.1
Corpus uteri	101	72.73	1.4[b]	36	29.42	1.2	15	9.19	1.6	3	1.90	1.6	168	125.13	1.3[b]
Uterus, NOS	9	12.97	0.7	5	3.75	1.3	3	0.81	3.7	0	0.15	0.0	17	20.12	0.8
Ovary, fallopian tubes	77	49.57	1.6[b]	34	18.49	1.8[b]	11	5.54	2.0	1	1.23	0.8	133	83.19	1.6[b]
Kidney, renal pelvis, ureter	15	17.06	0.9	2	6.91	0.3	2	2.40	0.8	0	0.59	0.0	21	29.77	0.7
Bladder, other urinary	37	30.99	1.2	18	12.82	1.4	1	4.65	0.2	2	1.37	1.5	62	54.87	1.1
Melanoma of the skin	20	13.09	1.5	4	4.80	0.8	3	1.53	2.0	2	0.36	5.6	33	21.99	1.5[b]
Eye	4	1.85	2.2	1	0.72	1.4	2	0.23	8.7	0	0.05	0.0	7	3.17	2.2
Brain, central nervous system	9	10.98	0.8	7	4.30	1.6	0	1.35	0.0	1	0.28	3.5	17	18.73	0.9
Thyroid gland	13	8.03	1.6	3	2.87	1.0	1	0.84	1.2	0	0.18	0.0	22	13.32	1.7[b]
Bone	0	1.61	0.0	1	0.54	1.9	0	0.16	0.0	0	0.04	0.0	2	2.64	0.8
Connective tissue	11	4.69	2.3[b]	1	1.76	0.6	2	0.55	3.6	0	0.14	0.0	14	7.94	1.8
Lymphatic, hematopoietic system	**51**	**70.16**	**0.7**[b]	**23**	**29.01**	**0.8**	**11**	**10.47**	**1.1**	**4**	**2.96**	**1.4**	**94**	**124.06**	**0.8**[b]
Non-Hodgkin's lymphoma	21	26.57	0.8	6	10.95	0.5	3	3.90	0.8	0	1.08	0.0	33	46.82	0.7[b]
Hodgkin's disease	5	4.91	1.0	1	1.84	0.5	1	0.58	1.7	0	0.11	0.0	7	8.29	0.8
Multiple myeloma	6	11.99	0.5	0	5.28	0.0[b]	2	2.05	1.0	2	0.60	3.3	12	21.83	0.5[b]
Leukemias	19	26.57	0.7	16	10.91	1.5	5	3.94	1.3	2	1.16	1.7	42	46.94	0.9
Chronic lymphocytic	1	7.41	0.1[b]	2	3.23	0.6	1	1.24	0.8	1	0.37	2.7	5	13.44	0.4[b]
Acute nonlymphocytic	11	8.83	1.2	4	3.72	1.1	4	1.40	2.9	0	0.43	0.0	19	15.81	1.2

[a] ICD-O code = 174.

[b] $P < .05$.

Second Cancer Following Cancer of the Female Genital System in Connecticut, 1935–82 [1]

Rochelle E. Curtis, [2] Robert N. Hoover, [3] Ruth A. Kleinerman, [2] *and* Elizabeth B. Harvey [2]

ABSTRACT—The risk of second primary cancer was evaluated in more than 25,000 women with cancer of the genital organs diagnosed between 1935 and 1982 in Connecticut. Significant excesses of subsequent cancers were observed following cancers of the cervix (35%, *n* = 656), uterine corpus (16%, *n* = 1,060), and ovary (58%, *n* = 366). When observed and expected second cancers of the female genital tract were excluded, these excesses became 40%, 30%, and 59% after cervix, uterine corpus, and ovary, respectively. Among women with either cancer of the cervix or uterine corpus, the risk of developing a second cancer rose with increasing duration of follow-up, reaching an excess of 61 and 34%, respectively, after 20 years. In contrast, among patients with ovarian cancer, the second cancer risk decreased over time to 41% after 10 years. Cancers related to smoking, i.e., oral cavity and pharynx, esophagus, and respiratory system, were notably increased among cervical cancer patients. The twofold to threefold risks observed for these second cancers are consistent with recent evidence linking cervical cancer to cigarette smoking and seem too large to be artifacts of confounding by low socioeconomic status. An increased incidence of second cancer of the abdominal organs (colon, rectum, kidney, bladder, ovaries) was generally observed for each gynecologic site. However, only rectal cancer was consistently linked with radiation treatment for the first primary cancer. Leukemia occurred in excess after cancers of the uterine corpus and ovary, but not after cervical cancer. The predominant cell type was acute nonlymphocytic leukemia, and the excess was associated with radiotherapy for uterine corpus cancer and with chemotherapy for ovarian cancer. Cancers of the breast and colon were increased following uterine corpus and ovarian cancer and vice versa, which supports the notion that these sites share a common etiology, perhaps related to dietary or hormonal factors. Cervical cancer patients experienced a deficit of subsequent breast cancer, possibly due to ovarian removal or ablation by radiation. Investigators need to explore further the association between the smoking-related cancer sites and cervical cancer, to clarify the role of radiotherapy and chemotherapy in relation to excess cancers, and to define more fully the etiologic factors that link cancers of the breast, colon, uterine corpus, and ovary.—Natl Cancer Inst Monogr 68: 113–137, 1985.

CERVIX (ICD-O, 180)

The incidence and mortality of invasive cervical cancer have been declining steadily at about 4% per year for all age groups from the 1940s through the 1970s in the United States (*1*). This decline has been attributed to the widespread use of the Papanicolaou smear, the increasing rate with which hysterectomies are being performed, and the general increase in the standard of living (*2*). Invasive cervical cancer accounted for 4% of all cancers diagnosed in females 1973–79 (*3*). Previously identified risk factors include early age at first coitus and first marriage, multiple sexual partners, and low socioeconomic status (*2*). The role of herpes virus type 2 and papillomavirus is under investigation, and cigarette smoking has also been implicated as a possible risk factor (*2, 4*). The 5-year relative survival rate for cervical cancer has improved over time from 58% in 1960–63 to 64% in 1970–73 (*5*). For localized disease, the 5-year survival rate was 82% in 1964–73.

Previous studies of second cancers following invasive cervical cancer have reported increased risks for cancers of the bladder, rectum, kidney, ovary, and uterine corpus in patients receiving radiotherapy (*6–9*). These risks were most noticeable among those followed for 15 or more years after treatment. Rates for lung cancer were also elevated, but not among long-term survivors. Surprisingly, large excesses of radiogenic leukemia, expected because of the high radiation dose to the bone marrow, have not been observed (*6, 8–11*). However, a small leukemia risk was recently reported from a large international survey (*7*).

Results

Between 1935 and 1982 in Connecticut, 8,086 women were diagnosed with a first primary invasive cancer of the uterine cervix and survived for at least 2 months. Almost 94% of these tumors were histologically confirmed. The average age at diagnosis was 52 years, and the average year of diagnosis was 1958. The women were followed for a total of 66,267 person-years after diagnosis, for an average follow-up of 8.2 years; 89% of the patients were either in active follow-up at the beginning of 1981 or were known to have died. Most cervical cancer patients in Connecticut received some form of radiotherapy as their initial treatment: Seventy percent of the women were

ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval; NOS = not otherwise specified; ANLL = acute nonlymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Radiation Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3A22, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Rochelle E. Curtis.

[3] Environmental Epidemiology Branch, Division of Cancer Etiology.

treated with radiation only, 10% with radiation and surgery, 16% with surgery only, and 4% with other treatments, including hormones and chemotherapy.

During the follow-up, 656 women were diagnosed with a second primary cancer compared with 485 expected based on rates prevailing in the general population (RR = 1.35; 95% CI = 1.25–1.46). The exclusion of the observed and expected second cervical cancers from the analysis increased the overall RR only marginally to 1.40; further exclusion of cancers of the uterine corpus, ovary, and other reproductive organs did not change this risk estimate. The RR of second primary cancer increased steadily and consistently with increasing duration of follow-up, rising from 0.9 within the first year of diagnosis to 1.6 among 20-year survivors. Among patients surviving 30 or more years, the RR reached 2.0.

The overall 35% excess of second primary tumors derived primarily from statistically significant RR of approximately twofold or greater for cancers of the oral cavity and pharynx (2.4), rectum (1.9), respiratory tract (3.5), kidney (2.0), and bladder (3.3). Nonsignificant elevations of similar magnitude were seen for cancers of the esophagus (RR = 2.3), connective tissue (RR = 2.3), and bone (RR = 2.7). A significant deficit (RR = 0.8) of breast cancer was also observed.

The risks for second cancers of the oral cavity, esophagus, stomach, and respiratory tract were elevated in practically all periods after cervical cancer diagnosis, and the RR did not increase over time. The frequency of subsequent rectal cancer was not initially increased over expectation, but the RR rose with increasing duration of follow-up. In contrast, the risk for second cancers of the kidney and bladder showed substantial elevations within the first 5 years, especially for bladder cancer, with even greater risks seen among long-term survivors (about sixfold for both sites in 30-year survivors). Also noteworthy was the unusually high RR of ovarian cancer among 30-year survivors (7.9, $n = 6$).

The data were also analyzed according to whether the patients received radiation therapy as part of their first course of treatment for cervical cancer. Because 80% of the women received radiation treatments, the opportunity to make meaningful comparisons with the small number of nonexposed women was restricted. However, risks of twofold to fourfold for cancers of the oral cavity, pharynx, and respiratory tract were seen in irradiated and nonirradiated patients. Two bone cancers occurred at 41 and 120 months following irradiation for cervical cancer, and both were located within the radiation field. The elevated RR for rectal cancer, particularly in long-term survivors, was limited to the irradiated patients. Second cancers of the kidney occurred at essentially normal levels in irradiated patients throughout the 1- to 19-year follow-up period, but then increased dramatically to approximately a sevenfold risk for 20-year survivors. In contrast, bladder cancer was elevated in every decade of follow-up, although the risks increased substantially 10 years posttreatment. Although 3.4 cancers were expected, no second primary tumors of the kidney and bladder were observed among the women who did not receive radiation treatment. All the excess risk of ovarian cancer in long-term survivors was concentrated among 30-year survivors who had received radiation treatment (RR = 7.9, $n = 5$). The RR for leukemia among the irradiated women was 1.2, and among 10-year survivors the observed number equaled that expected. The slight overall leukemia excess was derived from a twofold risk based on 4 observed cases occurring 5 to 9 years after treatment. The overall deficit of breast cancer was limited to the irradiated women (RR = 0.7). A small but nonsignificant excess of breast cancer occurred among those not irradiated (RR = 1.3). The deficit of breast cancer among the irradiated patients was apparent within the first year after the initial cervical cancer was diagnosed and remained reasonably consistent throughout the follow-up period.

Discussion

Patients with cervical cancer had an excess risk for second cancers of the oral cavity, pharynx, and respiratory system (including the nasal cavities, larynx, and lung). The magnitude of these risks was twofold to threefold and tended to be relatively constant over 30 years of follow-up among both the irradiated and nonirradiated women. Therefore, it is likely that these tumors share a common etiology with cervical cancer, rather than being related to treatment for the first primary. This would be consistent with the accumulating evidence linking cervical cancer to cigarette smoking because all these cancer sites are related to smoking habits. The link between smoking and cervical cancer was first suggested on the basis of concomitant geographic variation (*12*) and was recently supported by case-control studies (*13, 14*). The fact that women with cervical cancer are at high risk of developing cancers related to smoking adds further credibility to this hypothesis. Although the relationship could be simply an artifact due to an inverse association of all these cancers with socioeconomic indicators, this seems unlikely for two reasons. The twofold to threefold risks noted are greater than reported comparisons among the extremes of the socioeconomic gradient for the smoking-related sites (*15*). In addition, next to cervical cancer, the site with the strongest inverse relationship with social class is stomach cancer, and it is only marginally elevated (RR = 1.4) among patients with cervical cancer.

The excess risks for cancers of the rectum and bone appeared to follow a pattern consistent with radiation-induced second cancers. Both sites have been associated with ionizing radiation in other studies (*16*), and the excesses were generally restricted to irradiated women and to the later follow-up intervals. In addition, the high risk of ovarian cancer that appeared 30 years after treatment was confined to the irradiated patients, although ovarian cancer has not been consistently related to radiation (*16*). Nevertheless, these data are provocative when one considers that many women with cervical cancer have their ovaries surgically removed, so that the expected numbers of ovarian cancers should be considerably less than those based on the rates in the general population. The lack of any large excess risk of leukemia noted here is consistent with other cohort studies of cervical cancer patients (*10*). It has been speculated that the high doses of radiation to relatively small volumes of bone marrow may result in cell-killing rather than transformation. However, a slight elevation in leukemia risk was derived from the period when one might expect to see radiation-induced leukemias (5–9 yr following treatment). This could perhaps reflect the influence of lower doses of radiation absorbed by marrow outside the pelvis.

The elevated risks for bladder cancer and (to a lesser extent) kidney cancer were seen during the early and later stages of follow-up. Inasmuch as these women are closely monitored for cancer spread to the pelvic organs, the early excesses may be due to increased medical surveillance. The increased risks were seen only among the irradiated women, although small expected values among women not receiving radiation preclude any definite statement. The bladder probably received intense radiation exposure due to its location close to the cervix, whereas the kidneys, at an intermediate distance from the cervix, would have received lower doses (*7*). Both sites are apparently susceptible to radiogenic cancer, although previous studies have suggested that the level of excess risk is probably small (*16*). Kidney and bladder cancers have been associated with increased cigarette consumption (*17*), but the strength of the association to smoking is not of the magnitude to account for the threefold to fourfold RR developing after 10 years of follow-up. These data suggest that a combination of factors is responsible for the excess risk of urinary tract cancer, such as tobacco smoking, medical surveillance, radiation treatment, and possibly other factors.

The overall deficit of breast cancer among patients with cervical cancer was anticipated because the risk factors for one cancer tend to be protective for the other (*2*). The consistently reduced risk throughout the follow-up period would agree with this supposition, but the protective effect was confined to patients who had received radiation treatment. This may reflect the greater reduction in breast cancer risk associated with radiation castration compared with surgical castration noted in other studies (*7*), although the protective effects are present before the time that castration effects are usually noted (*18*), i.e., within the first 10 years of follow-up.

UTERINE CORPUS, UTERUS, NOT OTHERWISE SPECIFIED (ICD-O, 179, 182)

Cancer of the uterine corpus, including uterus, NOS, i.e., diagnoses not specified as to whether they originated in the cervix or corpus, is the third most common cancer in women, representing 9% of all newly diagnosed cancers (*3*). The incidence of uterine cancer remained constant until the early 1970s, when a sharp increase was observed, attributed mainly to the increasing use of menopausal estrogens (*1, 19*). Following public awareness of this problem and the consequent reduction in use of estrogens for menopausal symptoms, the incidence of uterine cancer began to decrease in the late 1970s (*1*). Major risk factors for uterine cancer relate to prolonged unopposed estrogen stimulation, obesity, late age at menopause, and nulliparity (*2, 20*). Less consistent associations have also been reported with diabetes, hypertension, prior pelvic radiation, and high socioeconomic status (*2, 21, 22*). Mortality rates have been declining over the years 1950–80, reflecting a combination of improved survival rates and earlier diagnoses. The 5-year relative survival rate for whites increased from 73% in 1960–63 to 81% in 1970–73 (*5*). Among white females, 78% of all cancers were localized to the corpus and survival was excellent: 90% at 5 years.

Previous surveys of uterine cancer have consistently revealed a 30 to 40% increased risk of subsequent breast cancer, the association being strongest for obese, nulliparous women, and a 40 to 90% excess risk for colorectal cancer (*6, 8, 23–26*). Less consistently, elevated risks have been noted for second leukemia (*27*), lymphoma (*24*), and cancers of the kidney (*8*), bladder (*24*), lung (*24, 26*), and thyroid (*25*). In addition, a significant deficit of stomach cancer has been reported (*8*).

Results

A total of 11,652 women survived 2 or more months after being diagnosed in Connecticut (1935–82) with cancers of the uterine corpus or uterus, NOS. The average age at diagnosis was 60 years, and the average year of diagnosis was 1964. These women were followed for a total of 95,367 person-years for an average of 8.2 years/patient. At the beginning of 1981, only 10% of the patients had been lost to follow-up. Women were generally treated with surgery alone (37%), surgery and radiation (40%), or radiotherapy alone (18%).

A total of 1,060 women developed a second primary cancer compared with 915 expected on the basis of incidence rates prevailing in the general population (RR = 1.16; 95% CI = 1.09–1.23). The treatment for uterine cancer often involves the resection of the entire female genital tract. Removing cancers of female reproductive organs from the risk analysis gives an overall RR of 1.30 (95% CI = 1.22–1.38). Most of the excess was due to statistically significant RR for cancers of the colon (1.4), rectum (1.6), lung (1.4), breast (1.3), kidney (2.1), bladder (1.7), and thyroid (2.0), and for leukemia (1.6). Also noteworthy were 60% nonsignificant excesses of multiple myeloma and cancers of the bone and connective tissue. Except for tumors of the female reproductive tract, no significant deficiencies of any cancer site were noted.

With second cancers of the genital tract removed from the total, fairly consistent excess risks of 23 to 35% were seen for the first 20 years after diagnosis of uterine cancer, beginning after the first year of follow-up. For those surviving 20 and more years, the risk increased to 50%. Of the individual sites increased above expectation, the RR for cancers of the colon and breast did not appear to follow any discernible pattern over time. Elevated risks for cancers of the lung and thyroid were limited to the first 20 years of follow-up; the lung cancer risk remained fairly constant at the 50–65% level over 20 years of follow-up after the first year, whereas the thyroid cancer excess was concentrated in the interval 10 to 19 years after diagnosis. The overall excess of leukemia was derived primarily from a twofold RR within the first 10 years of follow-up. Second primary cancers of the rectum, kidney, and bladder were all excessive within the first 5 years of follow-up and thereafter showed a general pattern of increasing RR over time. The risks among 20-year survivors were approximately twofold for cancer of the rectum and threefold to fourfold for cancers of the kidney and bladder. Increases for cancers of the bone and connective tissue were generally restricted to 10-year survivors. The observed number of ovarian cancers resembled that expected (35 vs. 41), which is notable given the frequency with which ovaries are removed during the treatment for cancer of the corpus uteri. This lack of anticipated "protection" against ovarian cancer was most pronounced within the first year following treatment (RR = 6.4, *n* = 22).

The RR of second primary tumors of the colon, breast, thyroid, kidney, bladder, and connective tissue were similar for those women whose initial treatment of uterine cancer included radiation and those who did not receive such treatment. The excess risks for multiple myeloma, rectal cancer, and bone cancer were concentrated in women who received radiation therapy and who survived 5 or more years. Cancers of the lung were seen more frequently in irradiated women; however, the excess appeared 1 year after the uterine corpus cancer diagnosis. Two bone cancers (both chondrosarcomas) occurred 10 or more years after radiation exposure; 1 developed in the pelvic region and the other in the long bones of the lower limb. Among irradiated women, the leukemia risk rose to twofold within 5 years of radiation therapy, remained at approximately this level for over 20 years, and was almost entirely due to ANLL. Patients not receiving radiation therapy experienced a subsequent leukemia risk similar to that of the general population, although their risk of chronic lymphocytic leukemia was unexplainably high.

The risk of second cancer among 905 women with a sarcoma of the uterine corpus was similar to that observed for all histologic types combined. Second cancers developed in 47 women at sites other than the female genital tract in comparison to 36.2 expected (RR = 1.30; 95% CI = 0.96–1.72; not shown in the table). Nonsignificant increased RR were found for second cancers of the rectum (2.6, *n* = 6), lung (2.2, *n* = 6), breast (1.2, *n* = 15), and thyroid (5.5, *n* = 2).

Discussion

For some time, it has been suspected that cancers of the uterine corpus, breast, and colon might share at least some common etiologic factors. The lines of human evidence are fourfold. The tumors vary concomitantly on a geographic basis (*28*), and migrant populations adopt (at varying rates) the risk of the nation to which they migrate (*29*). The tumors also appear to occur excessively over multiple generations among certain high-risk families (*30*). In addition, they tend to occur as complexes of multiple primary cancers (*8, 24–26*). This clustering was also confirmed by our study: Breast and colon cancers occurred excessively following cancer of the uterine corpus, and cancer of the uterine corpus occurred excessively following cancers of the colon and breast (*31, 32*). In addition, the excess risks appeared unrelated to radiation therapy and remained at approximately the same level in short- and long-term survivors. To date, the specific risk factors underlying this constellation of multiple cancers are uncertain, although dietary, hormonal, and genetic susceptibility factors are suspected (*2, 22, 33*). In addition, the current data suggest that cancers of the kidney, bladder, and thyroid also occur excessively after uterine corpus cancer. Similar associations have been reported by other investigators (*8, 24, 25*), who proposed the possibility of shared risk factors. The excesses were seen in irradiated and nonirradiated women and appeared within 5 years of the uterine corpus diagnosis. An alternative explanation for the increased risk of second cancers of the pelvic organs may be that the cancers are occult tumors discovered during the routine medical surveillance of these patients to detect spread of the initial cancer to contiguous or neighboring organs.

The excesses of leukemia, multiple myeloma, and cancers of the bone and rectum showed patterns that appeared consistent with a radiation etiology. These cancers have previously been associated with radiation (*16*), the excesses occurred primarily among women who were irradiated, and the bone marrow, pelvic bone, and rectum received substantial doses of radiation during the course of treatment for the uterine corpus cancer. The patterns of risk by time following radiation exposure were also consistent with other surveys of radiation-induced cancer at these sites (*16*).

The excess of ovarian cancer within a year following diagnosis of uterine corpus cancer and the excess risk of lung cancer over the first 20 years were unexpected. It could be that these increased risks are merely artifacts reflecting direct spread (ovary) and distant metastasis (lung) of cancers of the uterine corpus that were misdiagnosed as new primaries. However, because almost 80% of these patients have localized disease at diagnosis, it is unlikely that many of these patients would develop metastases to the lung. The ovarian excess could reflect the presence of estrogen-secreting tumors of the ovary, including theca cell and granulosa cell tumors, which might actually be responsible for the development of the cancers of the uterine corpus (*34*).

OVARY, FALLOPIAN TUBES, BROAD LIGAMENTS (ICD-O, 183)

Ovarian cancer is the fourth most frequent cause of cancer death among women in the United States and the leading cause of death from cancer of the female genital tract (*35*). On the basis of 1973–77 incidence rates from the Surveillance, Epidemiology, and End Results Program, about 1 of every 77 women will develop this cancer in their lifetime (*2*). Incidence and mortality rates for ovarian cancer have not changed substantially over the past four decades (*1*). Five-year relative survival rates have remained low over the past 20 years: 32% in 1960–63, 36% in 1970–73, and 37% in 1973–80 (*3*). This poor prognosis is related to the fact that most (70%) women have advanced disease at the time of diagnosis (*35*).

The only risk factor for ovarian cancer that has been reported consistently is never having been pregnant (*2*). Negative associations have been reported with increasing number of pregnancies and positive associations with increasing years of ovulation and family history of ovarian cancer (*2, 36*). Several studies have demonstrated an excess risk of leukemia following treatment of ovarian cancer with alkylating agents (*37–39*). Elevated risks of second cancers of the colon and bladder have also been linked to radiotherapy for ovarian cancer (*40*). Previous research has shown an increased risk for second cancers of the breast (*8, 25, 40, 41*) and uterine corpus (*8, 25, 40*). Excesses of cancers of the thyroid and lung have also been reported, although these were based on small numbers (*8, 25*).

Results

Over the years 1935–82 in Connecticut, 6,810 women survived 2 or more months after being diagnosed with a first primary cancer of the ovary. Their average age at diagnosis was 56 years, and the average year at diagnosis was 1963. These women were followed for a total of 31,200 person-years, for an average of 4.6 years per woman; 95% were either in active follow-up at the beginning of 1981 or had died. The first course of treatment for the ovarian cancer consisted of surgery only (33%), surgery and radiotherapy alone (36%), surgery and chemotherapy or chemotherapy alone (17%), radiotherapy and chemotherapy in combination (5%), or hormonal treatment only or no known treatment (9%).

Second primary cancers were reported in 366 women compared with approximately 232 that would have been expected based on the rates in the general population (RR = 1.58; 95% CI = 1.42–1.75). The overall RR estimate did not change when the 61 observed and 40 expected cases of cancers of the female genital tract were removed from the analysis. Most of the excess was accounted for by significantly increased RR for subsequent ANLL (5.4), and cancers of the colon (2.0), rectum (1.6), breast (1.4), uterine corpus (1.6), kidney (2.8), bladder (2.8) and connective tissue (5.0), plus nonsignificant elevations for cancers of the lung (1.6) and ovary (1.6).

The risk of second cancers was significantly elevated in all follow-up intervals, was highest within the first year after diagnosis of ovarian cancer (RR = 1.9), and progressively declined to 1.4 after 10 years. The excess risk within the first year of diagnosis was mainly attributable to excess cancers of the colon, lung, corpus uteri, rectum, and kidney. Because each of these sites represents a possible site of metastatic spread of ovarian cancer, or a site from which a cancer could spread to the ovary, the risks were reevaluated after elimination of the first year's data. Even after this procedure, substantial excess risks remained for each of these sites. The RR were 1.4, 1.5, 1.6, 1.7, and 2.5 for cancers of the corpus uteri, lung, rectum, colon, and kidney, respectively. With the exception of the first year of follow-up, the risks for cancers of the colon, rectum, and lung appeared to rise progressively with increasing follow-up, reaching risks of twofold or greater for each site among 10-year survivors. In contrast, the risks for breast cancer and cancer of the uterine corpus were highest during the first 5 years of follow-up and then dropped to essentially normal levels among 10-year survivors. Although based on small numbers, the overall excess of connective tissue cancer appeared to come mainly from 5 year survivors. Elevated risks for kidney and bladder cancer were inconsistent, being highest in the first 5 years of follow-up, then declining, and then rising again among 10-year survivors. Much of the kidney excess during the first 5 years after diagnosis was accounted for by 4 of 6 cancers discovered at autopsy. This pattern of excess second kidney cancers due to incidental autopsy findings was not found following initial cancers of the cervix and uterine corpus. The excess risk of leukemia and multiple myeloma was restricted to the time between 1 and 9 years after diagnosis of ovarian cancer, with 10-year survivors showing no excess. In addition, the fourfold to fivefold excess risk of leukemia seen within the first 10 years of follow-up could be attributed entirely to an approximately tenfold risk for ANLL.

The cancer sites showing excess risks were examined according to whether the patients received radiation as part of their initial course of treatment for ovarian cancer. Whereas risks were in excess for cancers of the colon, rectum, and lung among 10-year survivors who had not received radiotherapy, the RR were larger, and the trends with follow-up more pronounced for those who received radiation therapy, rising to twofold to threefold for each of these sites. The increased risks for thyroid cancer and connective tissue cancers among long-term survivors seemed restricted to those who had undergone radiation therapy. Two of the 3 sarcomas developing in irradiated women were located at sites within the radiation field, but the location of the third tumor was not specified in the tumor registry record. All 3 tumors occurred after approximately 20 years of follow-up.

Elevations of kidney cancer were similar in both irradiated and nonirradiated groups. Although the overall risk of bladder cancer was elevated in patients not treated with radiotherapy, a sevenfold excess (based on 6 cases) was seen among 10-year survivors who had received radiation therapy compared with a twofold risk for those who had not. Overall, an 80% excess risk of breast cancer was observed among the irradiated group that persisted 20 years following treatment for ovarian cancer. The breast cancer risk was more moderate in those who had not received radiation treatment and persisted only 5 years postdiagnosis of ovarian cancer before declining to the expected levels. Elevations of multiple myeloma and ANLL were present in both treatment groups, although higher RR were noted for those treated with radiation.

Based on indications from the literature, the risk of ANLL was evaluated according to whether the initial treatment for ovarian cancer included chemotherapy or not. Most of the excess risk could be explained by such treatment (RR = 43, *n* = 7). Two of the 7 patients received radiotherapy in addition to chemotherapy.

Discussion

Previous studies of multiple primary cancers have indicated associations between cancers of the ovary, breast, and uterine corpus (*8, 25, 40, 41*). This array of tumors also appeared in our series. Subsequent cancers of the uterine corpus and breast occurred 40 to 60% more frequently than expected among women with ovarian cancer. The excess risk of cancer of the uterine corpus is remarkable, given the fact that therapy for ovarian cancer frequently involves removal of the uterus. Because one would anticipate a deficiency of these neoplasms in ovarian cancer patients, the presence of a 60% excess risk suggests a strong association. However, it is noteworthy that in each case the interval between the diagnosis of the first ovarian and second uterine corpus primaries was less than 5 years, which raises the possibility that the elevation is due to misdiagnosed metastases. The increased risk for cancer of the breast tended to decline over time and approached normal levels among 10-year survivors. This pattern is consistent with the protective effects of ovarian ablation on cancers of the breast. Previous studies have indicated that it takes approximately 10 years for the protective effect of oophorectomy on breast cancer risk to become apparent (*18*). The association of these 3 types of cancers within the same patients is also consistent with their concomitant geographic variation (*28*) and lends credibility to the speculation that they share etiologic factors, perhaps dietary or hormonal in nature (*2, 36*).

After excluding the first year of follow-up, second cancers of the colon, rectum, lung, and connective tissue showed patterns of increasing risks with increasing time since the initial diagnosis of ovarian cancer and higher risks in irradiated versus nonirradiated patients. This suggests a radiation etiology. The high organ doses received and the associations reported in other epidemiologic studies support this interpretation for the cancers of the rectum and connective tissue (*7, 16*). Although patients with cancer of the colon have received substantial radiation doses, the colon has not been consistently identified as a radiosensitive organ in other studies (*7*); however, an apparent radiation effect was suggested among patients irradiated for ankylosing spondylitis (*42*). Lung cancer also has occurred excessively in several irradiated populations (*43*), but the excess in our study seemed high for the doses of radiation that the lung was likely to have absorbed. Radiation may have played a role in the sevenfold excess of second bladder cancer observed after 10 years of follow-up in irradiated women, although smaller increases were also seen in women not reported to be exposed to radiation. One difficulty in assessing the role of radiation-induced cancers in women with ovarian cancer is the fact that 70% of these patients were diagnosed with advanced disease, and, therefore, many of the women who did not receive radiation therapy for their initial treatment may have received such exposure in subsequent courses of treatment (*44*). Inasmuch as the only treatment information reported to the Registry is initial therapy, the radiation exposure of many patients may be misclassified.

Although the RR for second cancers of the pelvic organs were generally higher in patients exposed to radiation compared with women not receiving this therapy, some of the excess risks appear unrelated to treatment. The association of ovarian and colon cancer was reciprocal, i.e., ovarian cancer was also increased following colon cancer, which may suggest the presence of common etiologic factors. Moreover, pelvic area cancers may be diagnosed more frequently in patients with ovarian cancer due to the intensive medical screening these women receive so that physicians can detect spread of the initial cancer to contiguous sites. In addition, a portion of this excess may be accounted for by difficulty in distinguishing metastases from independent primaries.

Recent insights into the leukemogenic effects of several alkylating agents have come from analytic studies of the leukemia risks among ovarian cancer patients treated with these drugs (*37-39*). In line with this evidence, our study revealed a definite excess of ANLL within the first 10 years following treatment, primarily among those who received chemotherapy as part of their first course. This indicates the need for continued monitoring of these patients for risks of other tumors.

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CERVIX
FEMALES

TABLE 1A. *Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the cervix uteri, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	0	8,086	8,086
No. who developed a second primary cancer	0	656	656
Average age at diagnosis of first cancer, yr	0	52	52
Average yr of diagnosis of first cancer	0	1958	1958
Person-yr of follow-up	0	66,267	66,267
Average follow-up, yr	0.0	8.2	8.2
Percent given radiotherapy for first cancer	0.0	80.5	80.5

[a] ICD-O code = 180.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B. *Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the cervix uteri in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	533	81.3
Only the first cancer	81	12.3
Only the second cancer	37	5.6
Neither first nor second cancer	5	0.8
Total second primary cancers	656	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

CERVIX
FEMALES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the cervix uteri among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	8,086			6,534			3,741			2,533			8,086		
Person-yr in interval	6,041			18,750			15,292			26,183			66,267		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**30**	**32.19**	**0.9**	**137**	**105.59**	**1.3**[b]	**124**	**98.87**	**1.3**[b]	**365**	**248.23**	**1.5**[b]	**656**	**484.67**	**1.4**[b]
All excluding site of initial cancer	**30**	**30.27**	**1.0**	**137**	**99.80**	**1.4**[b]	**124**	**94.22**	**1.3**[b]	**362**	**241.07**	**1.5**[b]	**653**	**465.16**	**1.4**[b]
Buccal cavity, pharynx	**1**	**0.52**	**1.9**	**4**	**1.78**	**2.2**	**5**	**1.72**	**2.9**	**10**	**4.43**	**2.3**[b]	**20**	**8.45**	**2.4**[b]
Lip	0	0.03	0.0	0	0.10	0.0	1	0.09	10.6	0	0.25	0.0	1	0.48	2.1
Tongue	0	0.11	0.0	0	0.36	0.0	2	0.35	5.6	0	0.92	0.0	2	1.75	1.1
Salivary gland	0	0.08	0.0	1	0.26	3.8	0	0.23	0.0	0	0.53	0.0	1	1.10	0.9
Gum, other mouth	1	0.16	6.1	1	0.57	1.8	0	0.57	0.0	5	1.55	3.2[b]	7	2.85	2.5
Pharynx	0	0.12	0.0	2	0.42	4.8	2	0.41	4.9	5	1.01	4.9[b]	9	1.96	4.6[b]
Digestive system	**6**	**8.85**	**0.7**	**30**	**28.56**	**1.1**	**32**	**27.05**	**1.2**	**122**	**75.09**	**1.6**[b]	**190**	**139.49**	**1.4**[b]
Esophagus	0	0.19	0.0	3	0.63	4.7	1	0.61	1.6	3	1.68	1.8	7	3.11	2.3
Stomach	2	1.38	1.4	6	4.20	1.4	3	3.69	0.8	15	8.67	1.7	26	17.94	1.4
Colon	3	3.87	0.8	9	12.72	0.7	15	12.33	1.2	48	36.15	1.3	75	65.04	1.2
Rectum	1	1.76	0.6	8	5.75	1.4	5	5.44	0.9	39	14.57	2.7[b]	53	27.51	1.9[b]
Liver, biliary	0	0.63	0.0	0	1.98	0.0	2	1.83	1.1	6	4.85	1.2	8	9.28	0.9
Pancreas	0	0.80	0.0	3	2.62	1.1	4	2.54	1.6	7	7.76	0.9	14	13.72	1.0
Respiratory system	**5**	**1.47**	**3.4**[b]	**28**	**5.20**	**5.4**[b]	**24**	**5.25**	**4.6**[b]	**42**	**16.08**	**2.6**[b]	**99**	**27.99**	**3.5**[b]
Nasal cavities, sinuses	0	0.06	0.0	2	0.19	10.5[b]	0	0.18	0.0	1	0.41	2.4	3	0.84	3.6
Larynx	1	0.10	10.0	2	0.35	5.7	2	0.35	5.7	5	0.93	5.4[b]	10	1.74	5.7[b]
Trachea, bronchus, lung	4	1.29	3.1	24	4.58	5.2[b]	22	4.65	4.7[b]	36	14.54	2.5[b]	86	25.05	3.4[b]
Female breast	4	9.05	0.4	30	29.98	1.0	22	27.92	0.8	51	64.50	0.8	107	131.40	0.8[b]
Female genital tract	**7**	**6.72**	**1.0**	**13**	**21.58**	**0.6**	**23**	**19.27**	**1.2**	**56**	**40.23**	**1.4**[b]	**99**	**87.76**	**1.1**
Cervix uteri	0	1.92	0.0	0	5.79	0.0[b]	0	4.65	0.0[b]	3	7.16	0.4	3	19.51	0.2[b]
Corpus uteri	3	2.10	1.4	3	7.25	0.4	10	7.09	1.4	21	17.60	1.2	37	34.03	1.1
Uterus, NOS	1	0.67	1.5	1	1.92	0.5	2	1.50	1.3	4	2.09	1.9	8	6.18	1.3
Ovary, fallopian tubes	3	1.74	1.7	4	5.69	0.7	8	5.19	1.5	17	11.13	1.5	32	23.74	1.3
Kidney, renal pelvis, ureter	2	0.45	4.5	2	1.51	1.3	0	1.47	0.0	11	4.01	2.7[b]	15	7.44	2.0[b]
Bladder, other urinary	1	0.68	1.5	6	2.24	2.7	5	2.20	2.3	28	6.95	4.0[b]	40	12.07	3.3[b]
Melanoma of the skin	1	0.39	2.6	1	1.34	0.7	1	1.26	0.8	1	2.81	0.4	4	5.80	0.7
Eye	0	0.06	0.0	1	0.20	5.0	0	0.18	0.0	0	0.42	0.0	1	0.87	1.2
Brain, central nervous system	0	0.36	0.0	1	1.23	0.8	1	1.16	0.9	1	2.66	0.4	3	5.40	0.6
Thyroid gland	0	0.29	0.0	1	0.97	1.0	0	0.86	0.0	0	1.69	0.0	1	3.80	0.3
Bone	0	0.07	0.0	1	0.20	5.0	0	0.17	0.0	1	0.31	3.2	2	0.75	2.7
Connective tissue	0	0.16	0.0	2	0.52	3.9	1	0.45	2.2	2	1.01	2.0	5	2.14	2.3
Lymphatic, hematopoietic system	**2**	**1.78**	**1.1**	**9**	**5.96**	**1.5**	**7**	**5.77**	**1.2**	**17**	**16.57**	**1.0**	**35**	**30.08**	**1.2**
Non-Hodgkin's lymphoma	1	0.65	1.5	7	2.24	3.1[b]	1	2.20	0.5	7	6.26	1.1	16	11.34	1.4
Hodgkin's disease	0	0.20	0.0	0	0.62	0.0	1	0.54	1.9	1	1.14	0.9	2	2.49	0.8
Multiple myeloma	0	0.25	0.0	0	0.87	0.0	0	0.89	0.0	4	3.05	1.3	4	5.06	0.8
Leukemias	1	0.68	1.5	2	2.21	0.9	5	2.12	2.4	5	6.10	0.8	13	11.10	1.2
Chronic lymphocytic	0	0.15	0.0	0	0.52	0.0	0	0.53	0.0	2	1.81	1.1	2	3.01	0.7
Acute nonlymphocytic	0	0.21	0.0	1	0.70	1.4	0	0.68	0.0	0	2.09	0.0	1	3.68	0.3

[a] ICD-O code = 180.

[b] $P < .05$.

CERVIX
FEMALES
RADIOTHERAPY

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the cervix uteri among females given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,509			5,202			2,870			1,974			6,509		
Person-yr in interval	4,856			14,546			11,819			20,508			51,730		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**24**	**27.39**	**0.9**	**112**	**87.76**	**1.3**[b]	**102**	**80.86**	**1.3**[b]	**315**	**199.55**	**1.6**[b]	**553**	**395.39**	**1.4**[b]
All excluding site of initial cancer	**24**	**25.77**	**0.9**	**112**	**83.01**	**1.3**[b]	**102**	**77.10**	**1.3**[b]	**312**	**193.81**	**1.6**[b]	**550**	**379.53**	**1.4**[b]
Buccal cavity, pharynx	**1**	**0.44**	**2.3**	**4**	**1.47**	**2.7**	**3**	**1.39**	**2.2**	**7**	**3.49**	**2.0**	**15**	**6.79**	**2.2**[b]
Lip	0	0.03	0.0	0	0.09	0.0	1	0.08	12.5	0	0.20	0.0	1	0.40	2.5
Tongue	0	0.09	0.0	0	0.30	0.0	0	0.29	0.0	0	0.73	0.0	0	1.40	0.0
Salivary gland	0	0.07	0.0	1	0.21	4.7	0	0.19	0.0	0	0.43	0.0	1	0.90	1.1
Gum, other mouth	1	0.14	7.2	1	0.47	2.1	0	0.46	0.0	4	1.22	3.3	6	2.29	2.6
Pharynx	0	0.10	0.0	2	0.34	5.9	2	0.33	6.1	3	0.78	3.8	7	1.55	4.5[b]
Digestive system	**6**	**7.67**	**0.8**	**23**	**24.48**	**0.9**	**26**	**22.88**	**1.1**	**107**	**61.75**	**1.7**[b]	**162**	**116.74**	**1.4**[b]
Esophagus	0	0.17	0.0	3	0.54	5.6[b]	1	0.50	2.0	3	1.34	2.2	7	2.55	2.7[b]
Stomach	2	1.21	1.6	6	3.67	1.6	2	3.19	0.6	13	7.29	1.8	23	15.36	1.5
Colon	3	3.34	0.9	5	10.85	0.5	12	10.39	1.2	41	29.68	1.4	61	54.25	1.1
Rectum	1	1.53	0.7	6	4.90	1.2	4	4.56	0.9	36	11.88	3.0[b]	47	22.86	2.1[b]
Liver, biliary	0	0.55	0.0	0	1.72	0.0	1	1.57	0.6	4	4.05	1.0	5	7.89	0.6
Pancreas	0	0.69	0.0	3	2.24	1.3	4	2.15	1.9	6	6.34	0.9	13	11.42	1.1
Respiratory system	**3**	**1.23**	**2.4**	**27**	**4.22**	**6.4**[b]	**22**	**4.16**	**5.3**[b]	**34**	**12.45**	**2.7**[b]	**86**	**22.05**	**3.9**[b]
Nasal cavities, sinuses	0	0.05	0.0	2	0.16	12.5[b]	0	0.14	0.0	1	0.33	3.0	3	0.68	4.4
Larynx	0	0.08	0.0	2	0.28	7.1	1	0.28	3.6	4	0.72	5.6[b]	7	1.36	5.2[b]
Trachea, bronchus, lung	3	1.08	2.8	23	3.71	6.2[b]	21	3.68	5.7[b]	29	11.26	2.6[b]	76	19.72	3.9[b]
Female breast	3	7.61	0.4	17	24.41	0.7	16	22.31	0.7	36	51.06	0.7[b]	72	105.34	0.7[b]
Female genital tract	**5**	**5.73**	**0.9**	**12**	**17.88**	**0.7**	**21**	**15.67**	**1.3**	**53**	**32.04**	**1.7**[b]	**91**	**71.30**	**1.3**[b]
Cervix uteri	0	1.62	0.0	0	4.75	0.0[b]	0	3.76	0.0[b]	3	5.74	0.5	3	15.86	0.2[b]
Corpus uteri	2	1.79	1.1	3	5.98	0.5	10	5.72	1.7	20	13.82	1.4	35	27.30	1.3
Uterus, NOS	1	0.59	1.7	1	1.67	0.6	2	1.30	1.5	4	1.78	2.2	8	5.34	1.5
Ovary, fallopian tubes	2	1.48	1.4	4	4.70	0.9	7	4.19	1.7	16	8.86	1.8[b]	29	19.22	1.5[b]
Kidney, renal pelvis, ureter	2	0.38	5.2	2	1.27	1.6	0	1.22	0.0	11	3.23	3.4[b]	15	6.10	2.5[b]
Bladder, other urinary	1	0.58	1.7	6	1.90	3.2[b]	5	1.84	2.7	28	5.65	5.0[b]	40	9.96	4.0[b]
Melanoma of the skin	1	0.31	3.2	1	1.02	1.0	0	0.95	0.0	0	2.18	0.0	2	4.46	0.4
Eye	0	0.05	0.0	1	0.17	5.9	0	0.15	0.0	0	0.34	0.0	1	0.71	1.4
Brain, central nervous system	0	0.30	0.0	1	0.99	1.0	1	0.92	1.1	1	2.08	0.5	3	4.29	0.7
Thyroid gland	0	0.23	0.0	1	0.73	1.4	0	0.66	0.0	0	1.34	0.0	1	2.95	0.3
Bone	0	0.06	0.0	1	0.17	5.8	0	0.14	0.0	1	0.25	3.9	2	0.62	3.2
Connective tissue	0	0.14	0.0	1	0.42	2.4	1	0.37	2.7	1	0.81	1.2	3	1.74	1.7
Lymphatic, hematopoietic system	**1**	**1.51**	**0.7**	**8**	**4.94**	**1.6**	**5**	**4.74**	**1.1**	**17**	**13.44**	**1.3**	**31**	**24.63**	**1.3**
Non-Hodgkin's lymphoma	1	0.55	1.8	6	1.85	3.2[b]	0	1.79	0.0	7	5.02	1.4	14	9.21	1.5
Hodgkin's disease	0	0.16	0.0	0	0.49	0.0	1	0.43	2.3	1	0.91	1.1	2	1.99	1.0
Multiple myeloma	0	0.21	0.0	0	0.73	0.0	0	0.74	0.0	4	2.47	1.6	4	4.15	1.0
Leukemias	0	0.58	0.0	2	1.85	1.1	4	1.76	2.3	5	5.02	1.0	11	9.21	1.2
Chronic lymphocytic	0	0.13	0.0	0	0.44	0.0	0	0.44	0.0	2	1.49	1.3	2	2.50	0.8
Acute nonlymphocytic	0	0.17	0.0	1	0.57	1.8	0	0.55	0.0	0	1.70	0.0	1	2.99	0.3

[a] ICD-O code = 180.
[b] $P < .05$.

CERVIX
FEMALES
NO RADIOTHERAPY

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the cervix uteri among females not given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,577			1,332			871			559			1,577		
Person-yr in interval	1,185			4,204			3,473			5,675			14,537		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**6**	**4.79**	**1.3**	**25**	**17.83**	**1.4**	**22**	**18.01**	**1.2**	**50**	**48.68**	**1.0**	**103**	**89.28**	**1.2**
All excluding site of initial cancer	**6**	**4.50**	**1.3**	**25**	**16.79**	**1.5**	**22**	**17.12**	**1.3**	**50**	**47.26**	**1.1**	**103**	**85.63**	**1.2**
Buccal cavity, pharynx	**0**	**0.08**	**0.0**	**0**	**0.31**	**0.0**	**2**	**0.33**	**6.0**	**3**	**0.94**	**3.2**	**5**	**1.67**	**3.0**
Lip	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0	0	0.08	0.0
Tongue	0	0.02	0.0	0	0.06	0.0	2	0.07	29.0[b]	0	0.20	0.0	2	0.35	5.8
Salivary gland	0	0.01	0.0	0	0.05	0.0	0	0.04	0.0	0	0.10	0.0	0	0.21	0.0
Gum, other mouth	0	0.03	0.0	0	0.10	0.0	0	0.11	0.0	1	0.33	3.0	1	0.56	1.8
Pharynx	0	0.02	0.0	0	0.07	0.0	0	0.08	0.0	2	0.23	8.7	2	0.40	4.9
Digestive system	**0**	**1.17**	**0.0**	**7**	**4.08**	**1.7**	**6**	**4.17**	**1.4**	**15**	**13.34**	**1.1**	**28**	**22.75**	**1.2**
Esophagus	0	0.03	0.0	0	0.10	0.0	0	0.10	0.0	0	0.33	0.0	0	0.56	0.0
Stomach	0	0.17	0.0	0	0.53	0.0	1	0.50	2.0	2	1.38	1.4	3	2.58	1.2
Colon	0	0.53	0.0	4	1.87	2.1	3	1.94	1.5	7	6.46	1.1	14	10.79	1.3
Rectum	0	0.23	0.0	2	0.85	2.4	1	0.88	1.1	3	2.69	1.1	6	4.65	1.3
Liver, biliary	0	0.08	0.0	0	0.26	0.0	1	0.25	3.9	2	0.80	2.5	3	1.39	2.2
Pancreas	0	0.11	0.0	0	0.38	0.0	0	0.39	0.0	1	1.42	0.7	1	2.30	0.4
Respiratory system	**2**	**0.24**	**8.3**	**1**	**0.98**	**1.0**	**2**	**1.09**	**1.8**	**8**	**3.62**	**2.2**	**13**	**5.94**	**2.2**[b]
Nasal cavities, sinuses	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.08	0.0	0	0.16	0.0
Larynx	1	0.02	58.3	0	0.07	0.0	1	0.08	12.9	1	0.22	4.6	3	0.38	7.8[b]
Trachea, bronchus, lung	1	0.21	4.7	1	0.87	1.2	1	0.97	1.0	7	3.28	2.1	10	5.33	1.9
Female breast	1	1.45	0.7	13	5.57	2.3[b]	6	5.61	1.1	15	13.45	1.1	35	26.06	1.3
Female genital tract	**2**	**0.99**	**2.0**	**1**	**3.70**	**0.3**	**2**	**3.60**	**0.6**	**3**	**8.19**	**0.4**	**8**	**16.47**	**0.5**[b]
Cervix uteri	0	0.29	0.0	0	1.04	0.0	0	0.89	0.0	0	1.42	0.0	0	3.65	0.0
Corpus uteri	1	0.31	3.2	0	1.27	0.0	0	1.37	0.0	1	3.78	0.3	2	6.73	0.3
Uterus, NOS	0	0.08	0.0	0	0.25	0.0	0	0.21	0.0	0	0.31	0.0	0	0.84	0.0
Ovary, fallopian tubes	1	0.26	3.8	0	1.00	0.0	1	0.99	1.0	1	2.27	0.4	3	4.52	0.7
Kidney, renal pelvis, ureter	0	0.07	0.0	0	0.24	0.0	0	0.26	0.0	0	0.78	0.0	0	1.34	0.0
Bladder, other urinary	0	0.10	0.0	0	0.35	0.0	0	0.37	0.0	0	1.29	0.0	0	2.10	0.0
Melanoma of the skin	0	0.08	0.0	0	0.32	0.0	1	0.31	3.3	1	0.63	1.6	2	1.34	1.5
Eye	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.08	0.0	0	0.15	0.0
Brain, central nervous system	0	0.06	0.0	0	0.23	0.0	0	0.24	0.0	0	0.58	0.0	0	1.11	0.0
Thyroid gland	0	0.06	0.0	0	0.23	0.0	0	0.20	0.0	0	0.35	0.0	0	0.85	0.0
Bone	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.06	0.0	0	0.12	0.0
Connective tissue	0	0.03	0.0	1	0.10	10.5	0	0.09	0.0	1	0.19	5.1	2	0.40	5.0
Lymphatic, hematopoietic system	**1**	**0.28**	**3.6**	**1**	**1.02**	**1.0**	**2**	**1.03**	**1.9**	**0**	**3.13**	**0.0**	**4**	**5.45**	**0.7**
Non-Hodgkin's lymphoma	0	0.10	0.0	1	0.39	2.6	1	0.41	2.4	0	1.24	0.0	2	2.14	0.9
Hodgkin's disease	0	0.04	0.0	0	0.13	0.0	0	0.11	0.0	0	0.23	0.0	0	0.51	0.0
Multiple myeloma	0	0.04	0.0	0	0.14	0.0	0	0.15	0.0	0	0.58	0.0	0	0.91	0.0
Leukemias	1	0.10	10.0	0	0.36	0.0	1	0.36	2.8	0	1.08	0.0	2	1.89	1.1
Chronic lymphocytic	0	0.02	0.0	0	0.08	0.0	0	0.08	0.0	0	0.32	0.0	0	0.50	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.13	0.0	0	0.13	0.0	0	0.39	0.0	0	0.69	0.0

[a] ICD-O code = 180.

[b] $P < .05$.

CERVIX
FEMALES
LONG-TERM SURVIVORS

TABLE 1F.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the cervix uteri among females, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	6,534			2,533			1,173			323			8,086		
Person-yr in interval	34,043			17,807			6,884			1,493			66,267		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**261**	**204.39**	**1.3[b]**	**205**	**148.67**	**1.4[b]**	**116**	**77.47**	**1.5[b]**	**44**	**22.14**	**2.0[b]**	**656**	**484.67**	**1.4[b]**
All excluding site of initial cancer	**261**	**193.95**	**1.3[b]**	**204**	**143.55**	**1.4[b]**	**114**	**75.75**	**1.5[b]**	**44**	**21.82**	**2.0[b]**	**653**	**465.16**	**1.4[b]**
Buccal cavity, pharynx	**9**	**3.50**	**2.6[b]**	**7**	**2.69**	**2.6[b]**	**3**	**1.39**	**2.2**	**0**	**0.35**	**0.0**	**20**	**8.45**	**2.4[b]**
Lip	1	0.20	5.0	0	0.15	0.0	0	0.08	0.0	0	0.03	0.0	1	0.48	2.1
Tongue	2	0.72	2.8	0	0.56	0.0	0	0.29	0.0	0	0.07	0.0	2	1.75	1.1
Salivary gland	1	0.49	2.0	0	0.33	0.0	0	0.16	0.0	0	0.04	0.0	1	1.10	0.9
Gum, other mouth	1	1.13	0.9	2	0.92	2.2	3	0.50	6.0[b]	0	0.14	0.0	7	2.85	2.5
Pharynx	4	0.82	4.9[b]	5	0.64	7.8[b]	0	0.31	0.0	0	0.07	0.0	9	1.96	4.6[b]
Digestive system	**62**	**55.59**	**1.1**	**70**	**43.10**	**1.6[b]**	**38**	**24.29**	**1.6[b]**	**14**	**7.72**	**1.8**	**190**	**139.49**	**1.4[b]**
Esophagus	4	1.24	3.2	2	0.97	2.1	0	0.54	0.0	1	0.16	6.1	7	3.11	2.3
Stomach	9	7.89	1.1	9	5.26	1.7	6	2.63	2.3	0	0.78	0.0	26	17.94	1.4
Colon	24	25.04	1.0	30	20.33	1.5	14	11.89	1.2	4	3.94	1.0	75	65.04	1.2
Rectum	13	11.19	1.2	22	8.53	2.6[b]	10	4.65	2.2[b]	7	1.40	5.0[b]	53	27.51	1.9[b]
Liver, biliary	2	3.80	0.5	2	2.84	0.7	3	1.54	1.9	1	0.48	2.1	8	9.28	0.9
Pancreas	7	5.16	1.4	3	4.31	0.7	3	2.61	1.2	1	0.84	1.2	14	13.72	1.0
Respiratory system	**52**	**10.45**	**5.0[b]**	**32**	**9.02**	**3.5[b]**	**8**	**5.51**	**1.5**	**2**	**1.55**	**1.3**	**99**	**27.99**	**3.5[b]**
Nasal cavities, sinuses	2	0.37	5.5	1	0.25	3.9	0	0.13	0.0	0	0.03	0.0	3	0.84	3.6
Larynx	4	0.71	5.7[b]	3	0.56	5.3[b]	2	0.30	6.7	0	0.07	0.0	10	1.74	5.7[b]
Trachea, bronchus, lung	46	9.22	5.0[b]	28	8.09	3.5[b]	6	5.02	1.2	2	1.43	1.4	86	25.05	3.4[b]
Female breast	52	57.88	0.9	26	40.01	0.6[b]	19	19.37	1.0	6	5.13	1.2	107	131.40	0.8[b]
Female genital tract	**36**	**40.84**	**0.9**	**28**	**26.15**	**1.1**	**19**	**11.48**	**1.7**	**9**	**2.61**	**3.5[b]**	**99**	**87.76**	**1.1**
Cervix uteri	0	10.44	0.0[b]	1	5.12	0.2	2	1.72	1.2	0	0.32	0.0	3	19.51	0.2[b]
Corpus uteri	13	14.33	0.9	11	11.01	1.0	7	5.39	1.3	3	1.21	2.5	37	34.03	1.1
Uterus, NOS	3	3.43	0.9	2	1.56	1.3	2	0.44	4.5	0	0.08	0.0	8	6.18	1.3
Ovary, fallopian tubes	12	10.88	1.1	7	7.16	1.0	4	3.21	1.2	6	0.76	7.9[b]	32	23.74	1.3
Kidney, renal pelvis, ureter	2	2.98	0.7	2	2.34	0.9	7	1.31	5.4[b]	2	0.37	5.5	15	7.44	2.0[b]
Bladder, other urinary	11	4.45	2.5[b]	15	3.81	3.9[b]	8	2.35	3.4[b]	5	0.79	6.3[b]	40	12.07	3.3[b]
Melanoma of the skin	2	2.60	0.8	0	1.74	0.0	1	0.85	1.2	0	0.22	0.0	4	5.80	0.7
Eye	1	0.38	2.6	0	0.26	0.0	0	0.13	0.0	0	0.03	0.0	1	0.87	1.2
Brain, central nervous system	2	2.39	0.8	1	1.68	0.6	0	0.80	0.0	0	0.18	0.0	3	5.40	0.6
Thyroid gland	1	1.83	0.5	0	1.10	0.0	0	0.48	0.0	0	0.11	0.0	1	3.80	0.3
Bone	1	0.37	2.7	1	0.20	5.0	0	0.09	0.0	0	0.02	0.0	2	0.75	2.7
Connective tissue	3	0.97	3.1	0	0.63	0.0	1	0.30	3.4	1	0.08	12.1	5	2.14	2.3
Lymphatic, hematopoietic system	**16**	**11.73**	**1.4**	**10**	**9.40**	**1.1**	**5**	**5.43**	**0.9**	**2**	**1.74**	**1.1**	**35**	**30.08**	**1.2**
Non-Hodgkin's lymphoma	8	4.44	1.8	5	3.57	1.4	2	2.04	1.0	0	0.64	0.0	16	11.34	1.4
Hodgkin's disease	1	1.16	0.9	1	0.73	1.4	0	0.34	0.0	0	0.07	0.0	2	2.49	0.8
Multiple myeloma	0	1.76	0.0	1	1.64	0.6	1	1.06	0.9	2	0.35	5.6	4	5.06	0.8
Leukemias	7	4.33	1.6	3	3.44	0.9	2	2.00	1.0	0	0.67	0.0	13	11.10	1.2
Chronic lymphocytic	0	1.04	0.0	1	0.97	1.0	1	0.63	1.6	0	0.22	0.0	2	3.01	0.7
Acute nonlymphocytic	1	1.38	0.7	0	1.14	0.0	0	0.70	0.0	0	0.25	0.0	1	3.68	0.3

[a] ICD-O code = 180.

[b] $P < .05$.

CERVIX
FEMALES
LONG-TERM SURVIVORS
RADIOTHERAPY

Table 1G.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the cervix uteri among females given radiotherapy, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	5,202			1,974			906			258			6,509		
Person-yr in interval	26,366			13,914			5,353			1,241			51,730		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**214**	**168.56**	**1.3**^{b}	**180**	**119.97**	**1.5**^{b}	**98**	**61.07**	**1.6**^{b}	**37**	**18.55**	**2.0**^{b}	**553**	**395.39**	**1.4**^{b}
All excluding site of initial cancer	**214**	**160.06**	**1.3**^{b}	**179**	**115.87**	**1.5**^{b}	**96**	**59.70**	**1.6**^{b}	**37**	**18.28**	**2.0**^{b}	**550**	**379.53**	**1.4**^{b}
Buccal cavity, pharynx	**7**	**2.86**	**2.5**	**5**	**2.13**	**2.3**	**2**	**1.07**	**1.9**	**0**	**0.29**	**0.0**	**15**	**6.79**	**2.2**^{b}
Lip	1	0.17	5.9	0	0.12	0.0	0	0.06	0.0	0	0.02	0.0	1	0.40	2.5
Tongue	0	0.59	0.0	0	0.45	0.0	0	0.22	0.0	0	0.06	0.0	0	1.40	0.0
Salivary gland	1	0.40	2.5	0	0.26	0.0	0	0.13	0.0	0	0.04	0.0	1	0.90	1.1
Gum, other mouth	1	0.92	1.1	2	0.73	2.8	2	0.39	5.2	0	0.11	0.0	6	2.29	2.6
Pharynx	4	0.67	6.0^b	3	0.50	6.0^b	0	0.23	0.0	0	0.05	0.0	7	1.55	4.5^b
Digestive system	**49**	**47.35**	**1.0**	**62**	**35.66**	**1.7**^{b}	**33**	**19.57**	**1.7**^{b}	**12**	**6.53**	**1.8**	**162**	**116.74**	**1.4**^{b}
Esophagus	4	1.04	3.8^b	2	0.78	2.6	0	0.42	0.0	1	0.14	7.3	7	2.55	2.7^b
Stomach	8	6.86	1.2	7	4.46	1.6	6	2.17	2.8^b	0	0.67	0.0	23	15.36	1.5
Colon	17	21.24	0.8	26	16.78	1.5^b	12	9.58	1.3	3	3.33	0.9	61	54.25	1.1
Rectum	10	9.46	1.1	20	7.00	2.9^b	9	3.71	2.4^b	7	1.18	5.9^b	47	22.86	2.1^b
Liver, biliary	1	3.29	0.3	2	2.39	0.8	1	1.26	0.8	1	0.41	2.5	5	7.89	0.6
Pancreas	7	4.39	1.6	3	3.55	0.8	3	2.08	1.4	0	0.71	0.0	13	11.42	1.1
Respiratory system	**49**	**8.37**	**5.9**^{b}	**26**	**7.09**	**3.7**^{b}	**7**	**4.12**	**1.7**	**1**	**1.25**	**0.8**	**86**	**22.05**	**3.9**^{b}
Nasal cavities, sinuses	2	0.30	6.6	1	0.20	4.9	0	0.10	0.0	0	0.02	0.0	3	0.68	4.4
Larynx	3	0.56	5.4^b	2	0.44	4.6	2	0.22	9.0^b	0	0.06	0.0	7	1.36	5.2^b
Trachea, bronchus, lung	44	7.39	6.0^b	23	6.36	3.6^b	5	3.75	1.3	1	1.15	0.9	76	19.72	3.9^b
Female breast	33	46.71	0.7^b	19	31.69	0.6^b	11	15.09	0.7	6	4.28	1.4	72	105.34	0.7^b
Female genital tract	**33**	**33.55**	**1.0**	**27**	**20.92**	**1.3**	**19**	**8.96**	**2.1**^{b}	**7**	**2.16**	**3.2**^{b}	**91**	**71.30**	**1.3**^{b}
Cervix uteri	0	8.50	0.0^b	1	4.10	0.2	2	1.37	1.5	0	0.27	0.0	3	15.86	0.2^b
Corpus uteri	13	11.70	1.1	11	8.70	1.3	7	4.13	1.7	2	0.99	2.0	35	27.30	1.3
Uterus, NOS	3	2.97	1.0	2	1.33	1.5	2	0.37	5.4	0	0.07	0.0	8	5.34	1.5
Ovary, fallopian tubes	11	8.89	1.2	7	5.71	1.2	4	2.52	1.6	5	0.64	7.9^b	29	19.22	1.5^b
Kidney, renal pelvis, ureter	2	2.48	0.8	2	1.90	1.1	7	1.03	6.8^b	2	0.30	6.6	15	6.10	2.5^b
Bladder, other urinary	11	3.73	2.9^b	15	3.11	4.8^b	8	1.88	4.3^b	5	0.67	7.5^b	40	9.96	4.0^b
Melanoma of the skin	1	1.97	0.5	0	1.35	0.0	0	0.65	0.0	0	0.18	0.0	2	4.46	0.4
Eye	1	0.32	3.1	0	0.21	0.0	0	0.10	0.0	0	0.03	0.0	1	0.71	1.4
Brain, central nervous system	2	1.91	1.0	1	1.32	0.8	0	0.61	0.0	0	0.15	0.0	3	4.29	0.7
Thyroid gland	1	1.39	0.7	0	0.87	0.0	0	0.37	0.0	0	0.09	0.0	1	2.95	0.3
Bone	1	0.31	3.2	1	0.16	6.1	0	0.07	0.0	0	0.02	0.0	2	0.62	3.2
Connective tissue	2	0.79	2.5	0	0.51	0.0	1	0.24	4.2	0	0.07	0.0	3	1.74	1.7
Lymphatic, hematopoietic system	**13**	**9.68**	**1.3**	**10**	**7.65**	**1.3**	**5**	**4.32**	**1.2**	**2**	**1.48**	**1.4**	**31**	**24.63**	**1.3**
Non-Hodgkin's lymphoma	6	3.64	1.6	5	2.88	1.7	2	1.60	1.3	0	0.54	0.0	14	9.21	1.5
Hodgkin's disease	1	0.92	1.1	1	0.59	1.7	0	0.27	0.0	0	0.06	0.0	2	1.99	1.0
Multiple myeloma	0	1.47	0.0	1	1.33	0.8	1	0.84	1.2	2	0.30	6.6	4	4.15	1.0
Leukemias	6	3.62	1.7	3	2.83	1.1	2	1.62	1.2	0	0.57	0.0	11	9.21	1.2
Chronic lymphocytic	0	0.88	0.0	1	0.80	1.3	1	0.51	2.0	0	0.19	0.0	2	2.50	0.8
Acute nonlymphocytic	1	1.12	0.9	0	0.92	0.0	0	0.56	0.0	0	0.21	0.0	1	2.99	0.3

[a] ICD-O code = 180.

[b] $P < .05$.

CERVIX
FEMALES
LONG-TERM SURVIVORS
NO RADIOTHERAPY

TABLE 1H.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the cervix uteri among females not given radiotherapy, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	1,332			559			267			65			1,577		
Person-yr in interval	7,677			3,893			1,530			251			14,537		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**47**	**35.83**	**1.3**	**25**	**28.69**	**0.9**	**18**	**16.41**	**1.1**	**7**	**3.59**	**2.0**	**103**	**89.28**	**1.2**
All excluding site of initial cancer	**47**	**33.89**	**1.4**[b]	**25**	**27.68**	**0.9**	**18**	**16.06**	**1.1**	**7**	**3.54**	**2.0**	**103**	**85.63**	**1.2**
Buccal cavity, pharynx	**2**	**0.64**	**3.1**	**2**	**0.56**	**3.6**	**1**	**0.32**	**3.1**	**0**	**0.06**	**0.0**	**5**	**1.67**	**3.0**
Lip	0	0.03	0.0	0	0.03	0.0	0	0.01	0.0	0	0.00	0.0	0	0.08	0.0
Tongue	2	0.13	15.1[b]	0	0.12	0.0	0	0.07	0.0	0	0.01	0.0	2	0.35	5.8
Salivary gland	0	0.09	0.0	0	0.06	0.0	0	0.03	0.0	0	0.01	0.0	0	0.21	0.0
Gum, other mouth	0	0.21	0.0	0	0.19	0.0	1	0.12	8.7	0	0.02	0.0	1	0.56	1.8
Pharynx	0	0.16	0.0	2	0.14	14.3[b]	0	0.08	0.0	0	0.01	0.0	2	0.40	4.9
Digestive system	**13**	**8.24**	**1.6**	**8**	**7.44**	**1.1**	**5**	**4.72**	**1.1**	**2**	**1.19**	**1.7**	**28**	**22.75**	**1.2**
Esophagus	0	0.20	0.0	0	0.19	0.0	0	0.12	0.0	0	0.03	0.0	0	0.56	0.0
Stomach	1	1.03	1.0	2	0.80	2.5	0	0.46	0.0	0	0.11	0.0	3	2.58	1.2
Colon	7	3.80	1.8	4	3.55	1.1	2	2.31	0.9	1	0.61	1.7	14	10.79	1.3
Rectum	3	1.73	1.7	2	1.53	1.3	1	0.94	1.1	0	0.22	0.0	6	4.65	1.3
Liver, biliary	1	0.51	1.9	0	0.45	0.0	2	0.28	7.1	0	0.07	0.0	3	1.39	2.2
Pancreas	0	0.77	0.0	0	0.77	0.0	0	0.52	0.0	1	0.13	7.6	1	2.30	0.4
Respiratory system	**3**	**2.07**	**1.4**	**6**	**1.93**	**3.1**[b]	**1**	**1.39**	**0.7**	**1**	**0.30**	**3.3**	**13**	**5.94**	**2.2**[b]
Nasal cavities, sinuses	0	0.06	0.0	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.16	0.0
Larynx	1	0.15	6.8	1	0.13	7.8	0	0.08	0.0	0	0.01	0.0	3	0.38	7.8[b]
Trachea, bronchus, lung	2	1.84	1.1	5	1.73	2.9	1	1.27	0.8	1	0.28	3.6	10	5.33	1.9
Female breast	19	11.18	1.7[b]	7	8.31	0.8	8	4.29	1.9	0	0.85	0.0	35	26.06	1.3
Female genital tract	**3**	**7.30**	**0.4**	**1**	**5.23**	**0.2**	**0**	**2.52**	**0.0**	**2**	**0.44**	**4.5**	**8**	**16.47**	**0.5**[b]
Cervix uteri	0	1.94	0.0	0	1.01	0.0	0	0.35	0.0	0	0.05	0.0	0	3.65	0.0
Corpus uteri	0	2.63	0.0	0	2.31	0.0	0	1.26	0.0	1	0.22	4.6	2	6.73	0.3
Uterus, NOS	0	0.46	0.0	0	0.23	0.0	0	0.07	0.0	0	0.01	0.0	0	0.84	0.0
Ovary, fallopian tubes	1	1.99	0.5	0	1.45	0.0	0	0.70	0.0	1	0.13	7.8	3	4.52	0.7
Kidney, renal pelvis, ureter	0	0.50	0.0	0	0.44	0.0	0	0.28	0.0	0	0.06	0.0	0	1.34	0.0
Bladder, other urinary	0	0.71	0.0	0	0.70	0.0	0	0.48	0.0	0	0.12	0.0	0	2.10	0.0
Melanoma of the skin	1	0.63	1.6	0	0.39	0.0	1	0.20	5.0	0	0.04	0.0	2	1.34	1.5
Eye	0	0.06	0.0	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.15	0.0
Brain, central nervous system	0	0.47	0.0	0	0.36	0.0	0	0.18	0.0	0	0.04	0.0	0	1.11	0.0
Thyroid gland	0	0.44	0.0	0	0.23	0.0	0	0.10	0.0	0	0.02	0.0	0	0.85	0.0
Bone	0	0.06	0.0	0	0.04	0.0	0	0.02	0.0	0	0.00	0.0	0	0.12	0.0
Connective tissue	1	0.18	5.5	0	0.12	0.0	0	0.06	0.0	1	0.01	71.5	2	0.40	5.0
Lymphatic, hematopoietic system	**3**	**2.05**	**1.5**	**0**	**1.75**	**0.0**	**0**	**1.11**	**0.0**	**0**	**0.27**	**0.0**	**4**	**5.45**	**0.7**
Non-Hodgkin's lymphoma	2	0.80	2.5	0	0.69	0.0	0	0.44	0.0	0	0.11	0.0	2	2.14	0.9
Hodgkin's disease	0	0.24	0.0	0	0.14	0.0	0	0.07	0.0	0	0.01	0.0	0	0.51	0.0
Multiple myeloma	0	0.29	0.0	0	0.31	0.0	0	0.22	0.0	0	0.05	0.0	0	0.91	0.0
Leukemias	1	0.71	1.4	0	0.60	0.0	0	0.38	0.0	0	0.10	0.0	2	1.89	1.1
Chronic lymphocytic	0	0.16	0.0	0	0.17	0.0	0	0.12	0.0	0	0.03	0.0	0	0.50	0.0
Acute nonlymphocytic	0	0.26	0.0	0	0.22	0.0	0	0.14	0.0	0	0.04	0.0	0	0.69	0.0

[a] ICD-O code = 180.

[b] $P < .05$.

CORPUS
FEMALES

TABLE 2A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the corpus uteri or uterus, NOS, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	0	11,652	11,652
No. who developed a second primary cancer	0	1,060	1,060
Average age at diagnosis of first cancer, yr	0	60	60
Average yr of diagnosis of first cancer	0	1964	1964
Person-yr of follow-up	0	95,367	95,367
Average follow-up, yr	0.0	8.2	8.2
Percent given radiotherapy for first cancer	0.0	59.0	59.0

[a] ICD-O codes = 179, 182.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the corpus uteri or uterus, NOS in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	954	90.0
Only the first cancer	84	7.9
Only the second cancer	18	1.7
Neither first nor second cancer	4	0.4
Total second primary cancers	1,060	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

CORPUS
FEMALES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the corpus uteri or uterus, NOS among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	11,652			9,930			6,279			3,718			11,652		
Person-yr in interval	8,855			31,109			24,417			30,987			95,367		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**84**	**71.39**	**1.2**	**301**	**259.76**	**1.2**[b]	**260**	**224.85**	**1.2**[b]	**415**	**359.11**	**1.2**[b]	**1,060**	**914.64**	**1.2**[b]
All excluding site of initial cancer	**83**	**65.25**	**1.3**[b]	**301**	**237.50**	**1.3**[b]	**260**	**206.30**	**1.3**[b]	**415**	**333.69**	**1.2**[b]	**1,059**	**842.31**	**1.3**[b]
Buccal cavity, pharynx	**3**	**1.29**	**2.3**	**2**	**4.78**	**0.4**	**1**	**4.09**	**0.2**	**9**	**6.08**	**1.5**	**15**	**16.24**	**0.9**
Lip	1	0.07	13.9	0	0.26	0.0	0	0.22	0.0	0	0.39	0.0	1	0.94	1.1
Tongue	0	0.27	0.0	1	0.99	1.0	0	0.85	0.0	1	1.26	0.8	2	3.36	0.6
Salivary gland	1	0.16	6.3	1	0.57	1.8	0	0.49	0.0	1	0.76	1.3	3	1.97	1.5
Gum, other mouth	0	0.44	0.0	0	1.62	0.0	1	1.41	0.7	3	2.21	1.4	4	5.67	0.7
Pharynx	1	0.31	3.3	0	1.14	0.0	0	0.96	0.0	3	1.27	2.4	4	3.68	1.1
Digestive system	**18**	**20.63**	**0.9**	**104**	**74.74**	**1.4**[b]	**101**	**67.11**	**1.5**[b]	**154**	**118.55**	**1.3**[b]	**377**	**280.89**	**1.3**[b]
Esophagus	1	0.48	2.1	1	1.77	0.6	2	1.54	1.3	1	2.51	0.4	5	6.30	0.8
Stomach	2	2.75	0.7	11	9.53	1.2	9	8.22	1.1	11	13.79	0.8	33	34.29	1.0
Colon	7	9.46	0.7	50	34.62	1.4[b]	52	31.63	1.6[b]	83	57.78	1.4[b]	192	133.43	1.4[b]
Rectum	3	4.07	0.7	22	14.84	1.5	23	13.16	1.7[b]	38	22.12	1.7[b]	86	54.16	1.6[b]
Liver, biliary	1	1.39	0.7	5	4.95	1.0	6	4.43	1.4	6	7.80	0.8	18	18.56	1.0
Pancreas	4	2.04	2.0	13	7.48	1.7	5	6.80	0.7	13	12.42	1.0	35	28.74	1.2
Respiratory system	**2**	**4.46**	**0.4**	**26**	**17.06**	**1.5**	**21**	**14.96**	**1.4**	**31**	**22.97**	**1.3**	**80**	**59.43**	**1.3**[b]
Nasal cavities, sinuses	0	0.13	0.0	1	0.45	2.2	0	0.38	0.0	0	0.57	0.0	1	1.53	0.7
Larynx	0	0.28	0.0	1	1.04	1.0	1	0.87	1.1	0	1.21	0.0	2	3.40	0.6
Trachea, bronchus, lung	2	4.01	0.5	24	15.37	1.6[b]	20	13.53	1.5	31	20.93	1.5[b]	77	53.81	1.4[b]
Female breast	16	19.13	0.8	104	69.37	1.5[b]	72	58.35	1.2	105	87.30	1.2	297	234.01	1.3[b]
Female genital tract	**31**	**12.88**	**2.4**[b]	**10**	**46.04**	**0.2**[b]	**12**	**37.93**	**0.3**[b]	**11**	**51.60**	**0.2**[b]	**64**	**148.36**	**0.4**[b]
Cervix uteri	3	2.69	1.1	2	9.17	0.2[b]	1	7.06	0.1[b]	1	8.19	0.1[b]	7	27.10	0.3[b]
Corpus uteri	1	5.17	0.2	0	19.13	0.0[b]	0	16.19	0.0[b]	0	22.73	0.0[b]	1	63.19	0.0[b]
Uterus, NOS	0	0.97	0.0	0	3.13	0.0	0	2.36	0.0	0	2.69	0.0	0	9.14	0.0[b]
Ovary, fallopian tubes	22	3.43	6.4[b]	4	12.34	0.3[b]	7	10.31	0.7	2	14.46	0.1[b]	35	40.52	0.9
Kidney, renal pelvis, ureter	2	1.10	1.8	7	4.07	1.7	6	3.62	1.7	16	5.94	2.7[b]	31	14.72	2.1[b]
Bladder, other urinary	3	1.81	1.7	8	6.67	1.2	6	6.03	1.0	27	11.24	2.4[b]	44	25.73	1.7[b]
Melanoma of the skin	2	0.83	2.4	3	3.07	1.0	5	2.53	2.0	2	3.68	0.5	12	10.10	1.2
Eye	1	0.12	8.0	0	0.45	0.0	0	0.38	0.0	2	0.59	3.4	3	1.55	1.9
Brain, central nervous system	1	0.77	1.3	5	2.87	1.7	1	2.44	0.4	3	3.38	0.9	10	9.46	1.1
Thyroid gland	1	0.52	1.9	3	1.85	1.6	2	1.52	1.3	6	2.19	2.7[b]	12	6.07	2.0[b]
Bone	0	0.11	0.0	0	0.39	0.0	0	0.32	0.0	2	0.44	4.6	2	1.26	1.6
Connective tissue	0	0.30	0.0	0	1.08	0.0	2	0.92	2.2	4	1.42	2.8	6	3.73	1.6
Lymphatic, hematopoietic system	**3**	**4.32**	**0.7**	**18**	**16.02**	**1.1**	**24**	**14.48**	**1.7**[b]	**27**	**25.52**	**1.1**	**72**	**60.31**	**1.2**
Non-Hodgkin's lymphoma	0	1.66	0.0	4	6.24	0.6	7	5.61	1.2	6	9.40	0.6	17	22.90	0.7
Hodgkin's disease	0	0.33	0.0	0	1.20	0.0	1	1.02	1.0	2	1.51	1.3	3	4.06	0.7
Multiple myeloma	3	0.73	4.1	2	2.77	0.7	6	2.57	2.3	6	4.85	1.2	17	10.92	1.6
Leukemias	0	1.57	0.0	12	5.77	2.1[b]	10	5.25	1.9	13	9.74	1.3	35	22.32	1.6[b]
Chronic lymphocytic	0	0.43	0.0	4	1.60	2.5	3	1.50	2.0	4	2.99	1.3	11	6.51	1.7
Acute nonlymphocytic	0	0.51	0.0	4	1.93	2.1	4	1.77	2.3	3	3.33	0.9	11	7.54	1.5

[a] ICD-O codes = 179, 182.

[b] $P < .05$.

CORPUS
FEMALES
RADIOTHERAPY

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the corpus uteri or uterus, NOS among females given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,879			5,772			3,405			1,869			6,879		
Person-yr in interval	5,190			17,428			12,851			14,167			49,635		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**64**	**44.66**	**1.4**[b]	**188**	**155.98**	**1.2**[b]	**151**	**127.04**	**1.2**[b]	**204**	**173.74**	**1.2**[b]	**607**	**501.15**	**1.2**[b]
All excluding site of initial cancer	**63**	**40.84**	**1.5**[b]	**188**	**142.76**	**1.3**[b]	**151**	**116.82**	**1.3**[b]	**204**	**161.94**	**1.3**[b]	**606**	**462.13**	**1.3**[b]
Buccal cavity, pharynx	**1**	**0.81**	**1.2**	**1**	**2.89**	**0.3**	**0**	**2.31**	**0.0**	**2**	**2.88**	**0.7**	**4**	**8.89**	**0.4**
Lip	0	0.05	0.0	0	0.16	0.0	0	0.13	0.0	0	0.19	0.0	0	0.52	0.0
Tongue	0	0.17	0.0	1	0.59	1.7	0	0.48	0.0	0	0.60	0.0	1	1.84	0.5
Salivary gland	1	0.10	10.2	0	0.34	0.0	0	0.28	0.0	0	0.37	0.0	1	1.08	0.9
Gum, other mouth	0	0.28	0.0	0	0.99	0.0	0	0.80	0.0	0	1.05	0.0	0	3.12	0.0
Pharynx	0	0.19	0.0	0	0.69	0.0	0	0.53	0.0	1	0.58	1.7	1	1.99	0.5
Digestive system	**16**	**13.14**	**1.2**	**65**	**45.82**	**1.4**[b]	**61**	**38.82**	**1.6**[b]	**82**	**58.90**	**1.4**[b]	**224**	**156.60**	**1.4**[b]
Esophagus	0	0.31	0.0	1	1.09	0.9	2	0.89	2.3	1	1.23	0.8	4	3.51	1.1
Stomach	1	1.76	0.6	5	5.87	0.9	7	4.76	1.5	7	6.96	1.0	20	19.33	1.0
Colon	7	6.02	1.2	34	21.24	1.6[b]	25	18.37	1.4	41	28.75	1.4[b]	107	74.35	1.4[b]
Rectum	3	2.58	1.2	12	9.01	1.3	18	7.51	2.4[b]	22	10.85	2.0[b]	55	29.93	1.8[b]
Liver, biliary	1	0.89	1.1	4	3.04	1.3	4	2.57	1.6	4	3.91	1.0	13	10.41	1.2
Pancreas	4	1.31	3.0	7	4.63	1.5	3	3.97	0.8	6	6.16	1.0	20	16.07	1.2
Respiratory system	**2**	**2.86**	**0.7**	**20**	**10.52**	**1.9**[b]	**13**	**8.66**	**1.5**	**14**	**10.94**	**1.3**	**49**	**32.96**	**1.5**[b]
Nasal cavities, sinuses	0	0.08	0.0	1	0.27	3.8	0	0.22	0.0	0	0.28	0.0	1	0.84	1.2
Larynx	0	0.17	0.0	1	0.63	1.6	0	0.49	0.0	0	0.56	0.0	1	1.85	0.5
Trachea, bronchus, lung	2	2.57	0.8	18	9.50	1.9[b]	13	7.86	1.7	14	9.99	1.4	47	29.90	1.6[b]
Female breast	9	11.79	0.8	66	40.96	1.6[b]	34	32.36	1.1	43	41.44	1.0	152	126.47	1.2[b]
Female genital tract	**27**	**7.88**	**3.4**[b]	**5**	**26.88**	**0.2**[b]	**7**	**20.65**	**0.3**[b]	**5**	**24.02**	**0.2**[b]	**44**	**79.39**	**0.6**[b]
Cervix uteri	3	1.57	1.9	0	5.09	0.0[b]	0	3.66	0.0	0	3.72	0.0[b]	3	14.03	0.2[b]
Corpus uteri	1	3.23	0.3	0	11.41	0.0[b]	0	8.95	0.0[b]	0	10.48	0.0[b]	1	34.04	0.0[b]
Uterus, NOS	0	0.59	0.0	0	1.81	0.0	0	1.27	0.0	0	1.32	0.0	0	4.98	0.0[b]
Ovary, fallopian tubes	19	2.10	9.1[b]	2	7.20	0.3	4	5.62	0.7	1	6.76	0.1[b]	26	21.66	1.2
Kidney, renal pelvis, ureter	2	0.70	2.9	2	2.48	0.8	4	2.07	1.9	8	2.87	2.8[b]	16	8.11	2.0[b]
Bladder, other urinary	2	1.17	1.7	4	4.14	1.0	5	3.54	1.4	10	5.60	1.8	21	14.43	1.5
Melanoma of the skin	1	0.51	2.0	2	1.80	1.1	3	1.40	2.1	1	1.72	0.6	7	5.43	1.3
Eye	1	0.08	12.9	0	0.27	0.0	0	0.21	0.0	0	0.28	0.0	1	0.83	1.2
Brain, central nervous system	1	0.48	2.1	3	1.68	1.8	0	1.34	0.0	1	1.55	0.6	5	5.05	1.0
Thyroid gland	0	0.31	0.0	2	1.06	1.9	1	0.82	1.2	4	1.04	3.9[b]	7	3.23	2.2
Bone	0	0.07	0.0	0	0.23	0.0	0	0.18	0.0	2	0.21	9.5[b]	2	0.69	2.9
Connective tissue	0	0.19	0.0	0	0.64	0.0	1	0.51	2.0	2	0.69	2.9	3	2.02	1.5
Lymphatic, hematopoietic system	**2**	**2.72**	**0.7**	**10**	**9.71**	**1.0**	**17**	**8.30**	**2.0**[b]	**18**	**12.52**	**1.4**	**47**	**33.22**	**1.4**[b]
Non-Hodgkin's lymphoma	0	1.05	0.0	1	3.79	0.3	4	3.21	1.2	4	4.58	0.9	9	12.62	0.7
Hodgkin's disease	0	0.20	0.0	0	0.69	0.0	1	0.56	1.8	1	0.71	1.4	2	2.16	0.9
Multiple myeloma	2	0.47	4.3	1	1.70	0.6	5	1.49	3.4[b]	4	2.38	1.7	12	6.04	2.0[b]
Leukemias	0	0.99	0.0	8	3.50	2.3	7	3.02	2.3	9	4.85	1.9	24	12.35	1.9[b]
Chronic lymphocytic	0	0.27	0.0	2	0.99	2.0	0	0.88	0.0	1	1.49	0.7	3	3.63	0.8
Acute nonlymphocytic	0	0.32	0.0	4	1.17	3.4	4	1.02	3.9[b]	2	1.65	1.2	10	4.16	2.4[b]

[a] ICD-O codes = 179, 182.

[b] $P < .05$.

CORPUS
FEMALES
NO RADIOTHERAPY

TABLE 2E.– *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the corpus uteri or uterus, NOS among females not given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,773			4,158			2,874			1,849			4,773		
Person-yr in interval	3,665			13,681			11,566			16,820			45,732		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**20**	**26.73**	**0.7**	**113**	**103.78**	**1.1**	**109**	**97.81**	**1.1**	**211**	**185.37**	**1.1**	**453**	**413.50**	**1.1**
All excluding site of initial cancer	**20**	**24.41**	**0.8**	**113**	**94.73**	**1.2**	**109**	**89.48**	**1.2**[b]	**211**	**171.73**	**1.2**[b]	**453**	**380.19**	**1.2**[b]
Buccal cavity, pharynx	**2**	**0.48**	**4.2**	**1**	**1.89**	**0.5**	**1**	**1.78**	**0.6**	**7**	**3.20**	**2.2**	**11**	**7.35**	**1.5**
Lip	1	0.03	37.7	0	0.10	0.0	0	0.10	0.0	0	0.19	0.0	1	0.42	2.4
Tongue	0	0.10	0.0	0	0.39	0.0	0	0.37	0.0	1	0.66	1.5	1	1.52	0.7
Salivary gland	0	0.06	0.0	1	0.23	4.3	0	0.21	0.0	1	0.39	2.5	2	0.90	2.2
Gum, other mouth	0	0.16	0.0	0	0.64	0.0	1	0.60	1.7	3	1.15	2.6	4	2.55	1.6
Pharynx	1	0.11	8.8	0	0.46	0.0	0	0.43	0.0	2	0.69	2.9	3	1.69	1.8
Digestive system	**2**	**7.48**	**0.3**[b]	**39**	**28.92**	**1.3**	**40**	**28.29**	**1.4**[b]	**72**	**59.64**	**1.2**	**153**	**124.29**	**1.2**[b]
Esophagus	1	0.17	5.8	0	0.68	0.0	0	0.65	0.0	0	1.29	0.0	1	2.79	0.4
Stomach	1	0.99	1.0	6	3.67	1.6	2	3.47	0.6	4	6.83	0.6	13	14.95	0.9
Colon	0	3.44	0.0	16	13.38	1.2	27	13.27	2.0[b]	42	29.03	1.4[b]	85	59.08	1.4[b]
Rectum	0	1.50	0.0	10	5.82	1.7	5	5.65	0.9	16	11.27	1.4	31	24.23	1.3
Liver, biliary	0	0.50	0.0	1	1.91	0.5	2	1.86	1.1	2	3.89	0.5	5	8.15	0.6
Pancreas	0	0.73	0.0	6	2.86	2.1	2	2.83	0.7	7	6.26	1.1	15	12.68	1.2
Respiratory system	**0**	**1.61**	**0.0**	**6**	**6.54**	**0.9**	**8**	**6.30**	**1.3**	**17**	**12.03**	**1.4**	**31**	**26.46**	**1.2**
Nasal cavities, sinuses	0	0.05	0.0	0	0.18	0.0	0	0.17	0.0	0	0.30	0.0	0	0.69	0.0
Larynx	0	0.10	0.0	0	0.41	0.0	1	0.38	2.6	0	0.65	0.0	1	1.55	0.6
Trachea, bronchus, lung	0	1.44	0.0	6	5.87	1.0	7	5.68	1.2	17	10.94	1.6	30	23.91	1.3
Female breast	7	7.34	1.0	38	28.41	1.3	38	25.99	1.5[b]	62	45.85	1.4[b]	145	107.54	1.3[b]
Female genital tract	**4**	**4.99**	**0.8**	**5**	**19.15**	**0.3**[b]	**5**	**17.28**	**0.3**[b]	**6**	**27.58**	**0.2**[b]	**20**	**68.97**	**0.3**[b]
Cervix uteri	0	1.11	0.0	2	4.08	0.5	1	3.41	0.3	1	4.47	0.2	4	13.07	0.3[b]
Corpus uteri	0	1.94	0.0	0	7.73	0.0[b]	0	7.24	0.0[b]	0	12.26	0.0[b]	0	29.15	0.0[b]
Uterus, NOS	0	0.38	0.0	0	1.32	0.0	0	1.09	0.0	0	1.38	0.0	0	4.16	0.0[b]
Ovary, fallopian tubes	3	1.33	2.3	2	5.15	0.4	3	4.69	0.6	1	7.70	0.1[b]	9	18.86	0.5[b]
Kidney, renal pelvis, ureter	0	0.40	0.0	5	1.59	3.1[b]	2	1.54	1.3	8	3.06	2.6[b]	15	6.60	2.3[b]
Bladder, other urinary	1	0.65	1.5	4	2.52	1.6	1	2.49	0.4	17	5.64	3.0[b]	23	11.30	2.0[b]
Melanoma of the skin	1	0.33	3.1	1	1.26	0.8	2	1.13	1.8	1	1.95	0.5	5	4.67	1.1
Eye	0	0.05	0.0	0	0.18	0.0	0	0.17	0.0	2	0.31	6.4	2	0.71	2.8
Brain, central nervous system	0	0.30	0.0	2	1.19	1.7	1	1.10	0.9	2	1.83	1.1	5	4.42	1.1
Thyroid gland	1	0.21	4.9	1	0.79	1.3	1	0.70	1.4	2	1.15	1.7	5	2.84	1.8
Bone	0	0.04	0.0	0	0.16	0.0	0	0.14	0.0	0	0.23	0.0	0	0.57	0.0
Connective tissue	0	0.12	0.0	0	0.45	0.0	1	0.41	2.4	2	0.73	2.7	3	1.71	1.8
Lymphatic, hematopoietic system	**1**	**1.60**	**0.6**	**8**	**6.31**	**1.3**	**7**	**6.19**	**1.1**	**9**	**13.01**	**0.7**	**25**	**27.09**	**0.9**
Non-Hodgkin's lymphoma	0	0.61	0.0	3	2.45	1.2	3	2.40	1.3	2	4.82	0.4	8	10.28	0.8
Hodgkin's disease	0	0.13	0.0	0	0.51	0.0	0	0.46	0.0	1	0.81	1.2	1	1.91	0.5
Multiple myeloma	1	0.26	3.8	1	1.06	0.9	1	1.08	0.9	2	2.47	0.8	5	4.88	1.0
Leukemias	0	0.58	0.0	4	2.27	1.8	3	2.23	1.3	4	4.90	0.8	11	9.97	1.1
Chronic lymphocytic	0	0.15	0.0	2	0.61	3.3	3	0.62	4.8	3	1.50	2.0	8	2.88	2.8[b]
Acute nonlymphocytic	0	0.19	0.0	0	0.76	0.0	0	0.75	0.0	1	1.68	0.6	1	3.38	0.3

[a] ICD-O codes = 179, 182.

[b] $P < .05$.

CORPUS
FEMALES
LONG-TERM SURVIVORS

TABLE 2F.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the corpus uteri or uterus, NOS among females, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	9,930			3,718			1,232			280			11,652		
Person-yr in interval	55,525			23,003			6,831			1,153			95,367		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**561**	**484.46**	**1.2**[b]	**267**	**248.99**	**1.1**	**123**	**92.09**	**1.3**[b]	**25**	**18.08**	**1.4**	**1,060**	**914.64**	**1.2**[b]
All excluding site of initial cancer	**561**	**443.67**	**1.3**[b]	**267**	**230.28**	**1.2**[b]	**123**	**86.33**	**1.4**[b]	**25**	**17.12**	**1.5**	**1,059**	**842.31**	**1.3**[b]
Buccal cavity, pharynx	**3**	**8.87**	**0.3**[b]	**4**	**4.32**	**0.9**	**3**	**1.48**	**2.0**	**2**	**0.28**	**7.1**	**15**	**16.24**	**0.9**
Lip	0	0.48	0.0	0	0.26	0.0	0	0.10	0.0	0	0.02	0.0	1	0.94	1.1
Tongue	1	1.84	0.5	0	0.90	0.0	0	0.30	0.0	1	0.06	18.1	2	3.36	0.6
Salivary gland	1	1.06	0.9	1	0.53	1.9	0	0.19	0.0	0	0.04	0.0	3	1.97	1.5
Gum, other mouth	1	3.03	0.3	2	1.53	1.3	1	0.56	1.8	0	0.11	0.0	4	5.67	0.7
Pharynx	0	2.10	0.0	1	0.94	1.1	1	0.28	3.6	1	0.05	20.3	4	3.68	1.1
Digestive system	**205**	**141.81**	**1.4**[b]	**92**	**80.03**	**1.1**	**54**	**31.98**	**1.7**[b]	**8**	**6.56**	**1.2**	**377**	**280.89**	**1.3**[b]
Esophagus	3	3.31	0.9	0	1.72	0.0	0	0.66	0.0	1	0.14	7.4	5	6.30	0.8
Stomach	20	17.75	1.1	4	9.54	0.4	7	3.57	2.0	0	0.68	0.0	33	34.29	1.0
Colon	102	66.23	1.5[b]	49	38.52	1.3	31	15.93	1.9[b]	3	3.34	0.9	192	133.43	1.4[b]
Rectum	45	27.99	1.6[b]	25	15.16	1.6[b]	10	5.79	1.7	3	1.17	2.6	86	54.16	1.6[b]
Liver, biliary	11	9.38	1.2	4	5.33	0.8	2	2.06	1.0	0	0.41	0.0	18	18.56	1.0
Pancreas	18	14.28	1.3	8	8.28	1.0	4	3.43	1.2	1	0.72	1.4	35	28.74	1.2
Respiratory system	**47**	**32.01**	**1.5**[b]	**24**	**15.92**	**1.5**	**6**	**5.91**	**1.0**	**1**	**1.15**	**0.9**	**80**	**59.43**	**1.3**[b]
Nasal cavities, sinuses	1	0.83	1.2	0	0.41	0.0	0	0.14	0.0	0	0.02	0.0	1	1.53	0.7
Larynx	2	1.91	1.0	0	0.87	0.0	0	0.29	0.0	0	0.05	0.0	2	3.40	0.6
Trachea, bronchus, lung	44	28.89	1.5[b]	24	14.46	1.7[b]	6	5.42	1.1	1	1.06	0.9	77	53.81	1.4[b]
Female breast	176	127.67	1.4[b]	68	61.60	1.1	34	21.60	1.6[b]	3	4.10	0.7	297	234.01	1.3[b]
Female genital tract	**22**	**83.94**	**0.3**[b]	**8**	**37.90**	**0.2**[b]	**2**	**11.73**	**0.2**[b]	**1**	**1.99**	**0.5**	**64**	**148.36**	**0.4**[b]
Cervix uteri	3	16.23	0.2[b]	0	6.30	0.0[b]	1	1.65	0.6	0	0.25	0.0	7	27.10	0.3[b]
Corpus uteri	0	35.31	0.0[b]	0	16.61	0.0[b]	0	5.25	0.0[b]	0	0.88	0.0	1	63.19	0.0[b]
Uterus, NOS	0	5.48	0.0[b]	0	2.10	0.0	0	0.51	0.0	0	0.08	0.0	0	9.14	0.0[b]
Ovary, fallopian tubes	11	22.65	0.5[b]	1	10.51	0.1[b]	0	3.36	0.0	1	0.59	1.7	35	40.52	0.9
Kidney, renal pelvis, ureter	13	7.68	1.7	9	4.12	2.2	6	1.54	3.9[b]	1	0.28	3.6	31	14.72	2.1[b]
Bladder, other urinary	14	12.69	1.1	16	7.41	2.2[b]	5	3.14	1.6	6	0.69	8.7[b]	44	25.73	1.7[b]
Melanoma of the skin	8	5.59	1.4	1	2.60	0.4	1	0.91	1.1	0	0.18	0.0	12	10.10	1.2
Eye	0	0.83	0.0	1	0.42	2.4	1	0.14	6.9	0	0.03	0.0	3	1.55	1.9
Brain, central nervous system	6	5.31	1.1	3	2.49	1.2	0	0.77	0.0	0	0.13	0.0	10	9.46	1.1
Thyroid gland	5	3.37	1.5	6	1.57	3.8[b]	0	0.53	0.0	0	0.09	0.0	12	6.07	2.0[b]
Bone	0	0.71	0.0	1	0.32	3.1	1	0.10	10.3	0	0.02	0.0	2	1.26	1.6
Connective tissue	2	2.00	1.0	2	0.99	2.0	1	0.36	2.7	1	0.07	14.2	6	3.73	1.6
Lymphatic, hematopoietic system	**42**	**30.49**	**1.4**	**20**	**17.13**	**1.2**	**5**	**6.94**	**0.7**	**2**	**1.46**	**1.4**	**72**	**60.31**	**1.2**
Non-Hodgkin's lymphoma	11	11.85	0.9	5	6.38	0.8	0	2.50	0.0	1	0.52	1.9	17	22.90	0.7
Hodgkin's disease	1	2.22	0.5	2	1.11	1.8	0	0.35	0.0	0	0.05	0.0	3	4.06	0.7
Multiple myeloma	8	5.34	1.5	4	3.19	1.3	1	1.37	0.7	1	0.29	3.4	17	10.92	1.6
Leukemias	22	11.01	2.0[b]	9	6.43	1.4	4	2.72	1.5	0	0.59	0.0	35	22.32	1.6[b]
Chronic lymphocytic	7	3.09	2.3	1	1.94	0.5	3	0.86	3.5	0	0.19	0.0	11	6.51	1.7
Acute nonlymphocytic	8	3.70	2.2	2	2.17	0.9	1	0.95	1.1	0	0.22	0.0	11	7.54	1.5

[a] ICD-O codes = 179, 182.

[b] $P < .05$.

CORPUS
FEMALES
LONG-TERM SURVIVORS
RADIOTHERAPY

TABLE 2G.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the corpus uteri or uterus, NOS among females given radiotherapy, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	5,772			1,869			534			93			6,879		
Person-yr in interval	30,279			10,973			2,827			366			49,635		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	339	282.93	1.2[b]	132	127.62	1.0	64	40.16	1.6[b]	8	5.99	1.3	607	501.15	1.2[b]
All excluding site of initial cancer	339	259.50	1.3[b]	132	118.50	1.1	64	37.79	1.7[b]	8	5.69	1.4	606	462.13	1.3[b]
Buccal cavity, pharynx	1	5.20	0.2	1	2.16	0.5	1	0.63	1.6	0	0.09	0.0	4	8.89	0.4
Lip	0	0.28	0.0	0	0.14	0.0	0	0.05	0.0	0	0.01	0.0	0	0.52	0.0
Tongue	1	1.07	0.9	0	0.45	0.0	0	0.13	0.0	0	0.02	0.0	1	1.84	0.5
Salivary gland	0	0.61	0.0	0	0.27	0.0	0	0.08	0.0	0	0.01	0.0	1	1.08	0.9
Gum, other mouth	0	1.79	0.0	0	0.78	0.0	0	0.24	0.0	0	0.03	0.0	0	3.12	0.0
Pharynx	0	1.22	0.0	1	0.45	2.2	0	0.11	0.0	0	0.01	0.0	1	1.99	0.5
Digestive system	126	84.61	1.5[b]	48	42.34	1.1	31	14.33	2.2[b]	3	2.24	1.3	224	156.60	1.4[b]
Esophagus	3	1.97	1.5	0	0.89	0.0	0	0.29	0.0	1	0.05	22.2	4	3.51	1.1
Stomach	12	10.62	1.1	2	5.09	0.4	5	1.63	3.1	0	0.24	0.0	20	19.33	1.0
Colon	59	39.60	1.5[b]	25	20.46	1.2	15	7.16	2.1[b]	1	1.14	0.9	107	74.35	1.4[b]
Rectum	30	16.52	1.8[b]	13	7.90	1.6	8	2.55	3.1[b]	1	0.40	2.5	55	29.93	1.8[b]
Liver, biliary	8	5.61	1.4	3	2.84	1.1	1	0.93	1.1	0	0.14	0.0	13	10.41	1.2
Pancreas	10	8.59	1.2	4	4.39	0.9	2	1.53	1.3	0	0.24	0.0	20	16.07	1.2
Respiratory system	33	19.17	1.7[b]	11	8.11	1.4	3	2.49	1.2	0	0.34	0.0	49	32.96	1.5[b]
Nasal cavities, sinuses	1	0.48	2.1	0	0.21	0.0	0	0.06	0.0	0	0.01	0.0	1	0.84	1.2
Larynx	1	1.12	0.9	0	0.42	0.0	0	0.12	0.0	0	0.02	0.0	1	1.85	0.5
Trachea, bronchus, lung	31	17.35	1.8[b]	11	7.39	1.5	3	2.29	1.3	0	0.32	0.0	47	29.90	1.6[b]
Female breast	100	73.29	1.4[b]	26	30.86	0.8	16	9.25	1.7	1	1.34	0.7	152	126.47	1.2[b]
Female genital tract	12	47.52	0.3[b]	5	18.51	0.3[b]	0	4.89	0.0[b]	0	0.63	0.0	44	79.39	0.6[b]
Cervix uteri	0	8.75	0.0[b]	0	2.96	0.0	0	0.68	0.0	0	0.08	0.0	3	14.03	0.2[b]
Corpus uteri	0	20.35	0.0[b]	0	8.07	0.0[b]	0	2.14	0.0	0	0.27	0.0	1	34.04	0.0[b]
Uterus, NOS	0	3.08	0.0	0	1.05	0.0	0	0.23	0.0	0	0.03	0.0	0	4.98	0.0[b]
Ovary, fallopian tubes	6	12.82	0.5	1	5.16	0.2	0	1.41	0.0	0	0.19	0.0	26	21.66	1.2
Kidney, renal pelvis, ureter	6	4.55	1.3	5	2.12	2.4	3	0.67	4.5	0	0.09	0.0	16	8.11	2.0[b]
Bladder, other urinary	9	7.68	1.2	6	3.95	1.5	2	1.41	1.4	2	0.24	8.5	21	14.43	1.5
Melanoma of the skin	5	3.20	1.6	0	1.29	0.0	1	0.38	2.6	0	0.06	0.0	7	5.43	1.3
Eye	0	0.48	0.0	0	0.21	0.0	0	0.06	0.0	0	0.01	0.0	1	0.83	1.2
Brain, central nervous system	3	3.02	1.0	1	1.20	0.8	0	0.31	0.0	0	0.04	0.0	5	5.05	1.0
Thyroid gland	3	1.88	1.6	4	0.78	5.1[b]	0	0.22	0.0	0	0.03	0.0	7	3.23	2.2
Bone	0	0.41	0.0	1	0.16	6.1	1	0.04	24.0	0	0.01	0.0	2	0.69	2.9
Connective tissue	1	1.14	0.9	1	0.51	2.0	0	0.16	0.0	1	0.02	42.4	3	2.02	1.5
Lymphatic, hematopoietic system	27	18.00	1.5	14	8.96	1.6	3	3.07	1.0	1	0.49	2.0	47	33.22	1.4[b]
Non-Hodgkin's lymphoma	5	7.00	0.7	4	3.31	1.2	0	1.10	0.0	0	0.17	0.0	9	12.62	0.7
Hodgkin's disease	1	1.25	0.8	1	0.55	1.8	0	0.14	0.0	0	0.02	0.0	2	2.16	0.9
Multiple myeloma	6	3.19	1.9	2	1.68	1.2	1	0.60	1.7	1	0.10	10.1	12	6.04	2.0[b]
Leukemias	15	6.51	2.3[b]	7	3.42	2.0	2	1.22	1.6	0	0.21	0.0	24	12.35	1.9[b]
Chronic lymphocytic	2	1.86	1.1	0	1.04	0.0	1	0.38	2.6	0	0.07	0.0	3	3.63	0.8
Acute nonlymphocytic	8	2.19	3.7[b]	1	1.15	0.9	1	0.43	2.4	0	0.08	0.0	10	4.16	2.4[b]

[a] ICD-O codes = 179, 182.

[b] $P < .05$.

CORPUS
FEMALES
LONG-TERM SURVIVORS
NO RADIOTHERAPY

TABLE 2H.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the corpus uteri or uterus, NOS among females not given radiotherapy, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	4,158			1,849			698			187			4,773		
Person-yr in interval	25,247			12,030			4,004			786			45,732		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**222**	**201.53**	**1.1**	**135**	**121.37**	**1.1**	**59**	**51.94**	**1.1**	**17**	**12.09**	**1.4**	**453**	**413.50**	**1.1**
All excluding site of initial cancer	**222**	**184.15**	**1.2**[b]	**135**	**111.79**	**1.2**[b]	**59**	**48.55**	**1.2**	**17**	**11.43**	**1.5**	**453**	**380.19**	**1.2**[b]
Buccal cavity, pharynx	**2**	**3.67**	**0.5**	**3**	**2.16**	**1.4**	**2**	**0.85**	**2.3**	**2**	**0.19**	**10.4**[b]	**11**	**7.35**	**1.5**
Lip	0	0.20	0.0	0	0.12	0.0	0	0.05	0.0	0	0.02	0.0	1	0.42	2.4
Tongue	0	0.76	0.0	0	0.45	0.0	0	0.17	0.0	1	0.04	26.5	1	1.52	0.7
Salivary gland	1	0.44	2.3	1	0.26	3.8	0	0.11	0.0	0	0.02	0.0	2	0.90	2.2
Gum, other mouth	1	1.24	0.8	2	0.76	2.6	1	0.32	3.1	0	0.07	0.0	4	2.55	1.6
Pharynx	0	0.88	0.0	0	0.49	0.0	1	0.17	6.0	1	0.03	28.7	3	1.69	1.8
Digestive system	**79**	**57.20**	**1.4**[b]	**44**	**37.69**	**1.2**	**23**	**17.64**	**1.3**	**5**	**4.32**	**1.2**	**153**	**124.29**	**1.2**[b]
Esophagus	0	1.33	0.0	0	0.83	0.0	0	0.37	0.0	0	0.09	0.0	1	2.79	0.4
Stomach	8	7.13	1.1	2	4.45	0.4	2	1.94	1.0	0	0.45	0.0	13	14.95	0.9
Colon	43	26.64	1.6[b]	24	18.06	1.3	16	8.77	1.8[b]	2	2.20	0.9	85	59.08	1.4[b]
Rectum	15	11.47	1.3	12	7.27	1.7	2	3.24	0.6	2	0.77	2.6	31	24.23	1.3
Liver, biliary	3	3.77	0.8	1	2.49	0.4	1	1.13	0.9	0	0.27	0.0	5	8.15	0.6
Pancreas	8	5.69	1.4	4	3.89	1.0	2	1.90	1.1	1	0.47	2.1	15	12.68	1.2
Respiratory system	**14**	**12.84**	**1.1**	**13**	**7.81**	**1.7**	**3**	**3.42**	**0.9**	**1**	**0.80**	**1.2**	**31**	**26.46**	**1.2**
Nasal cavities, sinuses	0	0.35	0.0	0	0.20	0.0	0	0.08	0.0	0	0.02	0.0	0	0.69	0.0
Larynx	1	0.79	1.3	0	0.45	0.0	0	0.17	0.0	0	0.04	0.0	1	1.55	0.6
Trachea, bronchus, lung	13	11.54	1.1	13	7.07	1.8	3	3.13	1.0	1	0.74	1.3	30	23.91	1.3
Female breast	76	54.38	1.4[b]	42	30.74	1.4	18	12.36	1.5	2	2.76	0.7	145	107.54	1.3[b]
Female genital tract	**10**	**36.42**	**0.3**[b]	**3**	**19.39**	**0.2**[b]	**2**	**6.84**	**0.3**	**1**	**1.36**	**0.7**	**20**	**68.97**	**0.3**[b]
Cervix uteri	3	7.49	0.4	0	3.34	0.0	1	0.97	1.0	0	0.17	0.0	4	13.07	0.3[b]
Corpus uteri	0	14.97	0.0[b]	0	8.54	0.0[b]	0	3.11	0.0	0	0.61	0.0	0	29.15	0.0[b]
Uterus, NOS	0	2.41	0.0	0	1.04	0.0	0	0.28	0.0	0	0.05	0.0	0	4.16	0.0[b]
Ovary, fallopian tubes	5	9.83	0.5	0	5.35	0.0[b]	0	1.96	0.0	1	0.40	2.5	9	18.86	0.5[b]
Kidney, renal pelvis, ureter	7	3.14	2.2	4	2.00	2.0	3	0.88	3.4	1	0.19	5.2	15	6.60	2.3[b]
Bladder, other urinary	5	5.01	1.0	10	3.46	2.9[b]	3	1.73	1.7	4	0.45	8.9[b]	23	11.30	2.0[b]
Melanoma of the skin	3	2.40	1.3	1	1.31	0.8	0	0.53	0.0	0	0.12	0.0	5	4.67	1.1
Eye	0	0.35	0.0	1	0.21	4.7	1	0.08	11.8	0	0.02	0.0	2	0.71	2.8
Brain, central nervous system	3	2.29	1.3	2	1.29	1.6	0	0.46	0.0	0	0.09	0.0	5	4.42	1.1
Thyroid gland	2	1.48	1.3	2	0.79	2.5	0	0.30	0.0	0	0.06	0.0	5	2.84	1.8
Bone	0	0.30	0.0	0	0.16	0.0	0	0.06	0.0	0	0.01	0.0	0	0.57	0.0
Connective tissue	1	0.86	1.2	1	0.48	2.1	1	0.20	4.9	0	0.05	0.0	3	1.71	1.8
Lymphatic, hematopoietic system	**15**	**12.49**	**1.2**	**6**	**8.17**	**0.7**	**2**	**3.87**	**0.5**	**1**	**0.97**	**1.0**	**25**	**27.09**	**0.9**
Non-Hodgkin's lymphoma	6	4.85	1.2	1	3.07	0.3	0	1.40	0.0	1	0.35	2.8	8	10.28	0.8
Hodgkin's disease	0	0.97	0.0	1	0.56	1.8	0	0.21	0.0	0	0.04	0.0	1	1.91	0.5
Multiple myeloma	2	2.14	0.9	2	1.51	1.3	0	0.77	0.0	0	0.19	0.0	5	4.88	1.0
Leukemias	7	4.49	1.6	2	3.02	0.7	2	1.49	1.3	0	0.38	0.0	11	9.97	1.1
Chronic lymphocytic	5	1.23	4.1[b]	1	0.90	1.1	2	0.48	4.2	0	0.12	0.0	8	2.88	2.8[b]
Acute nonlymphocytic	0	1.51	0.0	1	1.02	1.0	0	0.52	0.0	0	0.14	0.0	1	3.38	0.3

[a] ICD-O codes = 179, 182.

[b] $P < .05$.

OVARY
FEMALES

TABLE 3A. *Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the ovary or fallopian tubes, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	0	6,810	6,810
No. who developed a second primary cancer	0	366	366
Average age at diagnosis of first cancer, yr	0	56	56
Average yr of diagnosis of first cancer	0	1963	1963
Person-yr of follow-up	0	31,200	31,200
Average follow-up, yr	0.0	4.6	4.6
Percent given radiotherapy for first cancer	0.0	40.6	40.6

[a] ICD-O code = 183.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the ovary or fallopian tubes in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	337	92.1
Only the first cancer	23	6.3
Only the second cancer	4	1.1
Neither first nor second cancer	2	0.6
Total second primary cancers	366	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

OVARY
FEMALES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the ovary or fallopian tubes among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,810			4,193			1,776			1,080			6,810		
Person-yr in interval	4,339			10,036			6,892			9,933			31,200		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**54**	**28.79**	**1.9**[b]	**109**	**64.82**	**1.7**[b]	**76**	**48.30**	**1.6**[b]	**127**	**89.79**	**1.4**[b]	**366**	**231.58**	**1.6**[b]
All excluding site of initial cancer	**54**	**27.34**	**2.0**[b]	**103**	**61.56**	**1.7**[b]	**70**	**45.94**	**1.5**[b]	**121**	**85.81**	**1.4**[b]	**348**	**220.54**	**1.6**[b]
Buccal cavity, pharynx	**1**	**0.52**	**1.9**	**1**	**1.17**	**0.9**	**2**	**0.89**	**2.3**	**1**	**1.65**	**0.6**	**5**	**4.22**	**1.2**
Lip	0	0.03	0.0	0	0.06	0.0	0	0.05	0.0	0	0.09	0.0	0	0.22	0.0
Tongue	1	0.11	9.5	0	0.24	0.0	1	0.18	5.5	0	0.34	0.0	2	0.87	2.3
Salivary gland	0	0.07	0.0	0	0.15	0.0	0	0.11	0.0	0	0.19	0.0	0	0.52	0.0
Gum, other mouth	0	0.17	0.0	1	0.40	2.5	1	0.30	3.3	1	0.58	1.7	3	1.45	2.1
Pharynx	0	0.12	0.0	0	0.28	0.0	0	0.21	0.0	0	0.38	0.0	0	1.00	0.0
Digestive system	**22**	**7.91**	**2.8**[b]	**25**	**17.55**	**1.4**	**19**	**13.29**	**1.4**	**45**	**26.35**	**1.7**[b]	**111**	**65.06**	**1.7**[b]
Esophagus	0	0.19	0.0	0	0.42	0.0	1	0.32	3.2	0	0.62	0.0	1	1.54	0.6
Stomach	1	1.03	1.0	5	2.21	2.3	3	1.60	1.9	0	2.92	0.0	9	7.75	1.2
Colon	17	3.65	4.7[b]	12	8.15	1.5	10	6.25	1.6	24	12.76	1.9[b]	63	30.80	2.0[b]
Rectum	3	1.58	1.9	2	3.52	0.6	4	2.66	1.5	12	5.13	2.3[b]	21	12.89	1.6[b]
Liver, biliary	0	0.52	0.0	2	1.14	1.8	0	0.85	0.0	4	1.66	2.4	6	4.17	1.4
Pancreas	0	0.78	0.0	3	1.74	1.7	1	1.34	0.7	4	2.75	1.5	8	6.60	1.2
Respiratory system	**4**	**1.78**	**2.2**	**2**	**4.06**	**0.5**	**5**	**3.10**	**1.6**	**11**	**6.36**	**1.7**	**22**	**15.30**	**1.4**
Nasal cavities, sinuses	0	0.05	0.0	0	0.11	0.0	0	0.08	0.0	0	0.14	0.0	0	0.39	0.0
Larynx	0	0.11	0.0	0	0.26	0.0	0	0.20	0.0	0	0.37	0.0	0	0.94	0.0
Trachea, bronchus, lung	4	1.59	2.5	2	3.64	0.5	5	2.79	1.8	11	5.78	1.9	22	13.79	1.6
Female breast	12	8.01	1.5	34	18.22	1.9[b]	16	13.41	1.2	25	23.72	1.1	87	63.33	1.4[b]
Female genital tract	**6**	**5.35**	**1.1**	**20**	**11.97**	**1.7**[b]	**19**	**8.65**	**2.2**[b]	**16**	**14.32**	**1.1**	**61**	**40.27**	**1.5**[b]
Cervix uteri	0	1.21	0.0	5	2.68	1.9	4	1.82	2.2	0	2.49	0.0	9	8.20	1.1
Corpus uteri	6	2.06	2.9[b]	5	4.70	1.1	7	3.55	2.0	8	6.40	1.3	26	16.69	1.6[b]
Uterus, NOS	0	0.38	0.0	4	0.78	5.1[b]	0	0.51	0.0	0	0.65	0.0	4	2.32	1.7
Ovary, fallopian tubes	0	1.45	0.0	6	3.26	1.8	6	2.36	2.5	6	3.98	1.5	18	11.04	1.6
Kidney, renal pelvis, ureter	2	0.43	4.6	4	0.97	4.1[b]	1	0.74	1.3	3	1.43	2.1	10	3.58	2.8[b]
Bladder, other urinary	1	0.69	1.4	5	1.56	3.2[b]	1	1.20	0.8	10	2.53	4.0[b]	17	5.97	2.8[b]
Melanoma of the skin	2	0.37	5.4	1	0.87	1.1	1	0.64	1.6	1	1.11	0.9	5	2.99	1.7
Eye	0	0.05	0.0	0	0.11	0.0	0	0.08	0.0	0	0.15	0.0	0	0.39	0.0
Brain, central nervous system	1	0.33	3.0	1	0.76	1.3	0	0.56	0.0	1	0.97	1.0	3	2.62	1.1
Thyroid gland	0	0.24	0.0	0	0.55	0.0	1	0.40	2.5	2	0.64	3.1	3	1.82	1.6
Bone	0	0.05	0.0	0	0.10	0.0	0	0.07	0.0	0	0.11	0.0	0	0.33	0.0
Connective tissue	1	0.13	7.8	0	0.29	0.0	1	0.21	4.7	3	0.36	8.3[b]	5	0.99	5.0[b]
Lymphatic, hematopoietic system	**0**	**1.73**	**0.0**	**13**	**3.94**	**3.3**[b]	**8**	**3.01**	**2.7**[b]	**4**	**6.01**	**0.7**	**25**	**14.68**	**1.7**[b]
Non-Hodgkin's lymphoma	0	0.67	0.0	1	1.52	0.7	2	1.16	1.7	1	2.32	0.4	4	5.67	0.7
Hodgkin's disease	0	0.15	0.0	1	0.35	2.8	0	0.25	0.0	0	0.41	0.0	1	1.16	0.9
Multiple myeloma	0	0.28	0.0	3	0.64	4.7	2	0.51	3.9	1	1.11	0.9	6	2.54	2.4
Leukemias	0	0.62	0.0	8	1.41	5.7[b]	4	1.08	3.7	2	2.17	0.9	14	5.28	2.7[b]
Chronic lymphocytic	0	0.16	0.0	0	0.37	0.0	0	0.29	0.0	2	0.64	3.1	2	1.47	1.4
Acute nonlymphocytic	0	0.21	0.0	6	0.49	12.3[b]	4	0.38	10.6[b]	0	0.77	0.0	10	1.84	5.4[b]

[a] ICD-O code = 183.

[b] $P < .05$.

OVARY
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TABLE 3D. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the ovary or fallopian tubes among females given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,767			1,758			741			422			2,767		
Person-yr in interval	1,822			4,117			2,811			3,457			12,208		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**18**	**10.76**	**1.7**	**48**	**24.99**	**1.9**[b]	**48**	**19.24**	**2.5**[b]	**59**	**30.82**	**1.9**[b]	**173**	**85.76**	**2.0**[b]
All excluding site of initial cancer	**18**	**10.17**	**1.8**[b]	**46**	**23.67**	**1.9**[b]	**45**	**18.27**	**2.5**[b]	**56**	**29.42**	**1.9**[b]	**165**	**81.48**	**2.0**[b]
Buccal cavity, pharynx	**0**	**0.19**	**0.0**	**1**	**0.47**	**2.1**	**0**	**0.38**	**0.0**	**1**	**0.59**	**1.7**	**2**	**1.63**	**1.2**
Lip	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.07	0.0
Tongue	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	0	0.12	0.0	0	0.34	0.0
Salivary gland	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.06	0.0	0	0.19	0.0
Gum, other mouth	0	0.06	0.0	1	0.16	6.4	0	0.13	0.0	1	0.21	4.8	2	0.56	3.6
Pharynx	0	0.05	0.0	0	0.12	0.0	0	0.09	0.0	0	0.14	0.0	0	0.40	0.0
Digestive system	**9**	**2.78**	**3.2**[b]	**11**	**6.27**	**1.8**	**12**	**4.84**	**2.5**[b]	**21**	**8.57**	**2.5**[b]	**53**	**22.45**	**2.4**[b]
Esophagus	0	0.07	0.0	0	0.16	0.0	0	0.13	0.0	0	0.22	0.0	0	0.56	0.0
Stomach	0	0.37	0.0	1	0.75	1.3	3	0.53	5.7[b]	0	0.89	0.0	4	2.52	1.6
Colon	7	1.27	5.5[b]	5	2.91	1.7	6	2.29	2.6	11	4.16	2.6[b]	29	10.62	2.7[b]
Rectum	1	0.57	1.8	1	1.30	0.8	2	1.00	2.0	6	1.72	3.5[b]	10	4.59	2.2[b]
Liver, biliary	0	0.18	0.0	1	0.39	2.6	0	0.29	0.0	2	0.52	3.9	3	1.38	2.2
Pancreas	0	0.27	0.0	2	0.63	3.2	1	0.50	2.0	1	0.91	1.1	4	2.31	1.7
Respiratory system	**0**	**0.60**	**0.0**	**1**	**1.60**	**0.6**	**3**	**1.41**	**2.1**	**5**	**2.42**	**2.1**	**9**	**6.03**	**1.5**
Nasal cavities, sinuses	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.15	0.0
Larynx	0	0.04	0.0	0	0.11	0.0	0	0.09	0.0	0	0.14	0.0	0	0.38	0.0
Trachea, bronchus, lung	0	0.53	0.0	1	1.43	0.7	3	1.27	2.4	5	2.20	2.3	9	5.43	1.7
Female breast	6	3.13	1.9	16	7.36	2.2[b]	10	5.57	1.8	13	8.32	1.6	45	24.37	1.8[b]
Female genital tract	**1**	**2.16**	**0.5**	**9**	**4.83**	**1.9**	**12**	**3.55**	**3.4**[b]	**7**	**5.06**	**1.4**	**29**	**15.60**	**1.9**[b]
Cervix uteri	0	0.53	0.0	1	1.09	0.9	2	0.71	2.8	0	0.86	0.0	3	3.19	0.9
Corpus uteri	1	0.81	1.2	3	1.94	1.5	6	1.54	3.9[b]	4	2.35	1.7	14	6.64	2.1[b]
Uterus, NOS	0	0.15	0.0	3	0.28	10.8[b]	0	0.17	0.0	0	0.19	0.0	3	0.79	3.8
Ovary, fallopian tubes	0	0.59	0.0	2	1.32	1.5	3	0.97	3.1	3	1.40	2.1	8	4.28	1.9
Kidney, renal pelvis, ureter	0	0.16	0.0	2	0.37	5.4	0	0.30	0.0	1	0.50	2.0	3	1.32	2.3
Bladder, other urinary	0	0.23	0.0	1	0.56	1.8	1	0.46	2.2	6	0.83	7.2[b]	8	2.08	3.9[b]
Melanoma of the skin	0	0.14	0.0	1	0.36	2.8	1	0.28	3.6	0	0.40	0.0	2	1.17	1.7
Eye	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.15	0.0
Brain, central nervous system	1	0.13	7.6	0	0.31	0.0	0	0.24	0.0	1	0.36	2.8	2	1.04	1.9
Thyroid gland	0	0.10	0.0	0	0.22	0.0	1	0.16	6.2	1	0.21	4.7	2	0.70	2.9
Bone	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0
Connective tissue	0	0.05	0.0	0	0.11	0.0	0	0.08	0.0	3	0.12	24.6[b]	3	0.37	8.2[b]
Lymphatic, hematopoietic system	**0**	**0.62**	**0.0**	**4**	**1.48**	**2.7**	**7**	**1.17**	**6.0**[b]	**0**	**2.02**	**0.0**	**11**	**5.28**	**2.1**[b]
Non-Hodgkin's lymphoma	0	0.24	0.0	0	0.58	0.0	1	0.47	2.1	0	0.81	0.0	1	2.09	0.5
Hodgkin's disease	0	0.06	0.0	1	0.14	7.1	0	0.10	0.0	0	0.14	0.0	1	0.44	2.3
Multiple myeloma	0	0.10	0.0	0	0.24	0.0	2	0.20	9.9[b]	0	0.38	0.0	2	0.92	2.2
Leukemias	0	0.22	0.0	3	0.51	5.8[b]	4	0.39	10.2[b]	0	0.70	0.0	7	1.82	3.8[b]
Chronic lymphocytic	0	0.06	0.0	0	0.13	0.0	0	0.11	0.0	0	0.21	0.0	0	0.50	0.0
Acute nonlymphocytic	0	0.07	0.0	1	0.18	5.5	4	0.14	27.7[b]	0	0.26	0.0	5	0.65	7.6[b]

[a] ICD-O code = 183.

[b] $P < .05$.

OVARY
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TABLE 3E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the ovary or fallopian tubes among females not given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,043			2,435			1,035			658			4,043		
Person-yr in interval	2,517			5,919			4,081			6,476			18,993		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**36**	**18.03**	**2.0**[b]	**61**	**39.83**	**1.5**[b]	**28**	**29.07**	**1.0**	**68**	**58.98**	**1.2**	**193**	**145.83**	**1.3**[b]
All excluding site of initial cancer	**36**	**17.16**	**2.1**[b]	**57**	**37.89**	**1.5**[b]	**25**	**27.68**	**0.9**	**65**	**56.40**	**1.2**	**183**	**139.06**	**1.3**[b]
Buccal cavity, pharynx	**1**	**0.32**	**3.1**	**0**	**0.70**	**0.0**	**2**	**0.51**	**3.9**	**0**	**1.06**	**0.0**	**3**	**2.60**	**1.2**
Lip	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.06	0.0	0	0.15	0.0
Tongue	1	0.07	15.2	0	0.14	0.0	1	0.10	9.6	0	0.22	0.0	2	0.53	3.8
Salivary gland	0	0.04	0.0	0	0.09	0.0	0	0.07	0.0	0	0.13	0.0	0	0.33	0.0
Gum, other mouth	0	0.11	0.0	0	0.24	0.0	1	0.17	5.8	0	0.37	0.0	1	0.90	1.1
Pharynx	0	0.08	0.0	0	0.16	0.0	0	0.12	0.0	0	0.24	0.0	0	0.59	0.0
Digestive system	**13**	**5.12**	**2.5**[b]	**14**	**11.28**	**1.2**	**7**	**8.45**	**0.8**	**24**	**17.78**	**1.3**	**58**	**42.61**	**1.4**[b]
Esophagus	0	0.12	0.0	0	0.26	0.0	1	0.19	5.3	0	0.41	0.0	1	0.98	1.0
Stomach	1	0.66	1.5	4	1.46	2.7	0	1.08	0.0	0	2.03	0.0	5	5.23	1.0
Colon	10	2.38	4.2[b]	7	5.24	1.3	4	3.96	1.0	13	8.61	1.5	34	20.18	1.7[b]
Rectum	2	1.01	2.0	1	2.22	0.4	2	1.65	1.2	6	3.42	1.8	11	8.30	1.3
Liver, biliary	0	0.34	0.0	1	0.75	1.3	0	0.56	0.0	2	1.15	1.7	3	2.79	1.1
Pancreas	0	0.51	0.0	1	1.11	0.9	0	0.83	0.0	3	1.84	1.6	4	4.30	0.9
Respiratory system	**4**	**1.18**	**3.4**	**1**	**2.46**	**0.4**	**2**	**1.69**	**1.2**	**6**	**3.94**	**1.5**	**13**	**9.27**	**1.4**
Nasal cavities, sinuses	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.09	0.0	0	0.24	0.0
Larynx	0	0.07	0.0	0	0.15	0.0	0	0.11	0.0	0	0.23	0.0	0	0.56	0.0
Trachea, bronchus, lung	4	1.07	3.8[b]	1	2.21	0.5	2	1.51	1.3	6	3.58	1.7	13	8.36	1.6
Female breast	6	4.88	1.2	18	10.86	1.7	6	7.84	0.8	12	15.40	0.8	42	38.96	1.1
Female genital tract	**5**	**3.19**	**1.6**	**11**	**7.14**	**1.5**	**7**	**5.10**	**1.4**	**9**	**9.25**	**1.0**	**32**	**24.67**	**1.3**
Cervix uteri	0	0.68	0.0	4	1.59	2.5	2	1.11	1.8	0	1.63	0.0	6	5.01	1.2
Corpus uteri	5	1.25	4.0[b]	2	2.76	0.7	1	2.01	0.5	4	4.05	1.0	12	10.06	1.2
Uterus, NOS	0	0.23	0.0	1	0.50	2.0	0	0.34	0.0	0	0.46	0.0	1	1.53	0.7
Ovary, fallopian tubes	0	0.87	0.0	4	1.94	2.1	3	1.39	2.2	3	2.58	1.2	10	6.77	1.5
Kidney, renal pelvis, ureter	2	0.28	7.3	2	0.60	3.3	1	0.45	2.2	2	0.94	2.1	7	2.25	3.1[b]
Bladder, other urinary	1	0.46	2.2	4	1.00	4.0[b]	0	0.75	0.0	4	1.70	2.4	9	3.90	2.3[b]
Melanoma of the skin	2	0.23	8.7	0	0.51	0.0	0	0.36	0.0	1	0.71	1.4	3	1.81	1.7
Eye	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.10	0.0	0	0.25	0.0
Brain, central nervous system	0	0.20	0.0	1	0.45	2.2	0	0.32	0.0	0	0.61	0.0	1	1.58	0.6
Thyroid gland	0	0.14	0.0	0	0.33	0.0	0	0.24	0.0	1	0.42	2.4	1	1.13	0.9
Bone	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.07	0.0	0	0.21	0.0
Connective tissue	1	0.08	12.8	0	0.18	0.0	1	0.13	7.7	0	0.24	0.0	2	0.63	3.2
Lymphatic, hematopoietic system	**0**	**1.11**	**0.0**	**9**	**2.46**	**3.7**[b]	**1**	**1.84**	**0.5**	**4**	**3.98**	**1.0**	**14**	**9.40**	**1.5**
Non-Hodgkin's lymphoma	0	0.43	0.0	1	0.94	1.1	1	0.69	1.4	1	1.51	0.7	3	3.57	0.8
Hodgkin's disease	0	0.09	0.0	0	0.21	0.0	0	0.15	0.0	0	0.27	0.0	0	0.73	0.0
Multiple myeloma	0	0.18	0.0	3	0.40	7.5[b]	0	0.31	0.0	1	0.73	1.4	4	1.62	2.5
Leukemias	0	0.40	0.0	5	0.90	5.5[b]	0	0.69	0.0	2	1.47	1.4	7	3.46	2.0
Chronic lymphocytic	0	0.11	0.0	0	0.24	0.0	0	0.19	0.0	2	0.44	4.6	2	0.96	2.1
Acute nonlymphocytic	0	0.14	0.0	5	0.31	16.4[b]	0	0.23	0.0	0	0.51	0.0	5	1.19	4.2[b]

[a] ICD-O code = 183.

[b] $P < .05$.

Second Cancer Following Cancer of the Male Genital System in Connecticut, 1935–82 [1]

Ruth A. Kleinerman,[2] Joan V. Liebermann,[2] *and* Frederick P. Li[3]

ABSTRACT—The risk of a second primary cancer developing was evaluated in nearly 20,000 men with cancers of the prostate or testis in Connecticut, 1935–82. Among 18,135 men with prostate cancer, a significant 15% deficit of all second cancers was observed [1,053 vs. 1,241; relative risk (RR) = 0.85; 95% CI = 0.80–0.90], most notably for respiratory (RR = 0.7) and digestive cancers (RR = 0.8). The absence of a colon cancer risk lends little support to the idea of common risk factors such as dietary fat consumption. Only the risk for salivary gland cancer was significantly increased, possibly due to chance. Leukemia was significantly elevated among men observed for 10 and more years (RR = 2.2). In contrast to most other index tumors, the prostate stands out as being associated with an overall low risk of second cancer development. The reasons for these deficiencies have not been explained. Among 1,446 men with testis cancer, a significant twofold risk of second cancers was seen (104 vs. 50.1). A fivefold risk of leukemia (8 vs. 1.5) was not related to treatment or age. Contralateral testis cancer (6 vs. 0.5) was elevated in men treated with and without radiation. Risks for kidney cancer (5 vs. 1.5), bladder cancer (9 vs. 3.4), pancreatic cancer (6 vs. 1.5), non-Hodgkin's lymphoma (6 vs. 1.5), and prostate cancer (12 vs. 5.9) were significantly increased. No trends over time were noted for any cancer. Overall risk of second cancer development tended to be higher in younger men with testis cancer. The relationship of leukemia to testis and prostate cancers should be investigated in future research.—Natl Cancer Inst Monogr 68: 139–147, 1985.

PROSTATE (ICD-O, 185)

The prostate gland is one of the most common cancer sites in males. Because the incidence increases progressively with age (*1*), prostate cancer occurs primarily in men older than 50 years of age. Prostate cancer accounts for 18% of all male cancers, and the age-adjusted incidence has increased 51% from 1935 to 1965 in Connecticut (*2*). Among men with prostate cancer, 61% presented with localized disease, 13% with regional disease, and 21% with distant disease (*3*). Among white males, the 5-year relative survival rate has increased from 50% in 1960–63 to 68% in 1973–80 (*3*). Incidence rates are higher among blacks than whites in the United States. The risk factors are obscure, but current hypotheses include endogenous androgens, sexually transmitted viruses, nutritional factors (e.g., dietary fat), and industrial exposures to zinc and cadmium (*1, 2, 4*).

An earlier survey of prostate cancer in Connecticut in 1935–64 revealed significant deficits of cancers of the esophagus, stomach, colon, liver, and lung. Significant excesses were observed for leukemia and other male genital organs, excluding the testes (*5*). Simultaneous cancers of the prostate and other genitourinary organs have also been reported (*6, 7*).

Results

Over the years 1935 to 1982, a total of 18,135 males with prostate cancer were reported to the Connecticut Tumor Registry. The average age at diagnosis was 72 years, and the average year of diagnosis was 1967. Average follow-up was 3.9 years. Excluding the prostate as the site of a second tumor, 1,053 second cancers developed compared with 1,241 cancers expected on the basis of general population rates (RR = 0.85; 95% CI = 0.80–0.90). This 15% deficit persisted throughout the entire follow-up period. However, for men under 65 years of age, risk of second cancers was equal to that expected (1.0, 95% CI = 0.9–1.1).

Significant deficits of second cancers affected mainly the lung (RR = 0.7; *n* = 182) and the digestive tract (RR = 0.8; *n* = 422), including the esophagus (RR = 0.5; *n* = 15), stomach (RR = 0.7; *n* = 61), and colon (RR = 0.9; *n* = 174). Risks for cancer of the brain (RR = 0.2; *n* = 2), gum and mouth (0.5; *n* = 9), and a second prostate cancer (0.0; *n* = 1) were especially low. The only significant excess was noted for cancer of the salivary glands (RR = 2.7; 95% CI = 1.3–4.8), although leukemia was of borderline significance (RR = 1.3; 95% CI = 1.0–1.6). Among 10-year survivors, the only significant excess was for leukemia (RR = 2.2).

Discussion

The deficit of second tumors following prostate cancer should be noted, especially in contrast with most other index cancers in this monograph for which few deficits are observed. The absence of an excess risk of colon cancer argues against the hypothesis that dietary fat intake may be a common etiologic factor (*1*). A relationship between prostate and other genitourinary cancers (*6, 7*) also appears unlikely because no excess of bladder or kidney

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Abbreviations: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Radiation Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3A22, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Ruth A. Kleinerman.

[3] Clinical Epidemiology Branch, Division of Cancer Etiology.

cancers following prostate cancer was observed. Previous associations with other genitourinary cancers may have resulted from detection bias (*4*), involving tumors of the same organ system. The virtual absence of second tumors of the prostate is due to the fact that most patients underwent prostatectomy.

An explanation for several of these observations is difficult. The small excess of salivary gland tumors was not predicted and may be due to chance. Prostate cancer was not elevated after salivary cancer, as reported elsewhere in this monograph (*8*). The excess of leukemia among 10-year survivors is notable because all cases occurred among men not treated with radiation and was approximately twofold for both ANLL and chronic lymphocytic leukemia. The relationship between prostate cancer and leukemia is bidirectional (*9*), which suggests the influence of a common risk factor. However, patients dying with leukemia have higher than average rates of autopsy that likely contributed to the high proportion of prostate cancer reported. The reasons for the low risk of second cancers of the digestive and respiratory systems developing deserve further study, especially because smoking habits among prostate cancer patients are reported to be similar to those of other men (*2*). Because most of the deficits of second cancers were confirmed to men 65 years of age and older, it is possible that second cancers are not sought and diagnosed in elderly patients with prostate cancer.

TESTIS (ICD-O, 186)

Testis cancer occurs primarily in young men aged 25 to 34 years and is more common in whites than blacks in the United States (*10*). Among males under age 29 years in Connecticut, testis cancer incidence has doubled from the 1940s to the 1970s (*11*) but has declined among elderly men. Undescended testis or cryptorchidism has been identified as a major risk factor for testis cancer, and incidence of this cancer appears to be higher among men of high social class (*12*). The 5-year relative survival has improved from 63% in 1960–63 to 72% in 1970–73 (*13*). Survival rates have increased largely because of improved therapy for men with disseminated testis cancer other than seminoma, which primarily affects men 20 to 29 years old (*14*). Treatment is related to cell type and usually consists of surgery followed by radiation for seminomas and surgery followed by combination chemotherapy for nonseminomas. Use of radiation and chemotherapy has raised concerns that leukemia might develop as a late effect (*15, 16*).

Previous studies have indicated approximately twofold increased risks of second cancers following testis cancer (*5, 17, 18*). Elevations in risk have been reported for leukemia, contralateral testis cancer, transitional cell cancers of the urinary tract, and cancers of the colon, pharynx, and liver.

Results

Between 1935 and 1982, the Connecticut Tumor Registry received notices that 1,446 men developed testis cancer. The average age at diagnosis was 35 years, and the average year of diagnosis was 1965. Radiation was received by 58% of the testis cancer patients. The average follow-up was 8 years, and 104 patients developed a second cancer, compared with 50.1 expected (RR = 2.08; 95% CI = 1.70–2.52). This twofold risk was consistent over all the years studied and was seen for irradiated and nonirradiated men. Eight leukemias were observed versus 1.5 expected (RR = 5.2; 95% CI = 2.3–10). Risks were also significantly elevated for malignant tumors of connective tissue (3 vs. 0.4), contralateral testis (6 vs. 0.5), pancreas (6 vs. 1.5), prostate (12 vs. 5.9), kidney (5 vs. 1.5), bladder (9 vs. 3.4), and non-Hodgkin's lymphoma (6 vs. 1.5). Patterns of increased risk over time for these cancers were not consistent.

Among 977 men under 40 years of age at the time their testis cancer was diagnosed, a threefold risk of developing second cancers was observed (3.0; 95% CI = 2.2–4.1). Of the 469 patients 40 years or older, the RR for second cancers was 1.7 (95% CI = 1.3–2.1).

Discussion

The twofold risk of second cancers among men with testis cancer that occurred consistently across all study periods and in both irradiated and nonirradiated treatment groups is similar to previous reports (*5, 17, 18*). Patients less than 40 years of age at diagnosis of testis cancer were at twice the risk of developing a second cancer compared with older men with testis cancer followed for the same duration. Although the risk was based on only 8 cases, leukemia occurred in excess. Complete treatment data were available for 6 of 8 cases (Kleinerman RA: Unpublished observations). However, radiation treatment was unlikely to be a major factor because leukemias occurred in both irradiated and nonirradiated groups. Two of the men with ANLL received alkylating agents, a known cause of leukemia (*19*). Two previous surveys have also indicated significant risks for leukemia following testis cancer (*5, 18*). Furthermore, the relationship between testis cancer and leukemia is bidirectional (*9*). A predisposition to leukemia among testis cancer patients due to a shared etiologic factor cannot be excluded and makes any risk associated with chemotherapy difficult for one to evaluate. Risk of cancer of the contralateral testis was also elevated and tended to be diagnosed 1–9 years after the initial testis cancer. Almost all the second testis cancers were of different cell types from the first.

Aside from leukemia and contralateral testis cancer, statistically significant risks for other cancers tended to be confined to either the irradiated or the nonirradiated group. Among the irradiated group, the risks for cancers of the lung, pancreas, bladder, and kidney were elevated. Excess cancers of these sites suggest a relationship to smoking because no increased risks over time were noted in the manner of radiation-induced cancers. However, none of these cancer sites showed increased risks in the nonirradiated group, and the smoking habits of patients with testis cancer are not reported to be increased. In the nonirradiated group, significantly elevated risks were noted for cancers of the prostate and connective tissue and non-Hodgkin's lymphomas, but these were based on small numbers of observed cases. Because treatment for testis cancer is specific to cell type, it is possible that the histology as well as treatment of testis cancer may affect the risk of some subsequent neoplasms.

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PROSTATE
MALES

TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the prostate gland, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	18,135	0	18,135
No. who developed a second primary cancer	1,054	0	1,054
Average age at diagnosis of first cancer, yr	72	0	72
Average yr of diagnosis of first cancer	1967	0	1967
Person-yr of follow-up	70,358	0	70,358
Average follow-up, yr	3.9	0.0	3.9
Percent given radiotherapy for first cancer	12.5	0.0	12.5

[a] ICD-O code = 185.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the prostate gland in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	855	81.1
Only the first cancer	110	10.4
Only the second cancer	74	7.0
Neither first nor second cancer	15	1.4
Total second primary cancers	1,054	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

PROSTATE
MALES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the prostate gland among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	18,135			14,645			5,154			1,563			18,135		
Person-yr in interval	13,405			35,720			14,889			6,344			70,358		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**161**	**276.92**	**0.6**[b]	**534**	**784.89**	**0.7**[b]	**229**	**361.84**	**0.6**[b]	**130**	**176.49**	**0.7**[b]	**1,054**	**1,598.88**	**0.7**[b]
All excluding site of initial cancer	**161**	**217.59**	**0.7**[b]	**533**	**612.72**	**0.9**[b]	**229**	**278.93**	**0.8**[b]	**130**	**133.20**	**1.0**	**1,053**	**1,241.45**	**0.8**[b]
Buccal cavity, pharynx	**10**	**12.43**	**0.8**	**31**	**33.89**	**0.9**	**13**	**14.77**	**0.9**	**6**	**6.50**	**0.9**	**60**	**67.53**	**0.9**
Lip	5	2.51	2.0	4	6.79	0.6	4	3.01	1.3	4	1.35	3.0	17	13.64	1.2
Tongue	0	2.39	0.0	7	6.46	1.1	2	2.77	0.7	1	1.16	0.9	10	12.76	0.8
Salivary gland	2	0.71	2.8	6	2.00	3.0[b]	2	0.94	2.1	1	0.48	2.1	11	4.12	2.7[b]
Gum, other mouth	1	3.43	0.3	7	9.38	0.7	1	4.06	0.2	0	1.77	0.0	9	18.63	0.5[b]
Pharynx	2	2.87	0.7	7	7.87	0.9	2	3.40	0.6	0	1.48	0.0	11	15.61	0.7
Digestive system	**60**	**89.99**	**0.7**[b]	**205**	**252.69**	**0.8**[b]	**105**	**115.83**	**0.9**	**52**	**55.73**	**0.9**	**422**	**513.83**	**0.8**[b]
Esophagus	2	5.40	0.4	7	14.76	0.5[b]	4	6.37	0.6	2	2.77	0.7	15	29.27	0.5[b]
Stomach	15	16.65	0.9	24	45.51	0.5[b]	16	20.35	0.8	6	9.44	0.6	61	91.88	0.7[b]
Colon	26	34.79	0.7	83	99.54	0.8	41	46.67	0.9	24	23.44	1.0	174	204.28	0.9[b]
Rectum	6	18.05	0.3[b]	55	50.44	1.1	27	22.93	1.2	8	10.72	0.7	96	102.05	0.9
Liver, biliary	0	4.61	0.0[b]	10	13.01	0.8	4	6.00	0.7	5	2.93	1.7	19	26.52	0.7
Pancreas	11	9.02	1.2	20	25.43	0.8	12	11.71	1.0	4	5.59	0.7	47	51.71	0.9
Respiratory system	**30**	**49.90**	**0.6**[b]	**108**	**140.83**	**0.8**[b]	**50**	**62.90**	**0.8**	**23**	**28.85**	**0.8**	**211**	**282.26**	**0.7**[b]
Nasal cavities, sinuses	1	0.58	1.7	5	1.62	3.1	1	0.75	1.3	0	0.36	0.0	7	3.31	2.1
Larynx	2	5.13	0.4	15	13.94	1.1	4	5.93	0.7	1	2.47	0.4	22	27.45	0.8
Trachea, bronchus, lung	27	43.75	0.6[b]	88	124.01	0.7[b]	45	55.67	0.8	22	25.78	0.9	182	249.00	0.7[b]
Prostate gland	0	59.33	0.0[b]	1	172.17	0.0[b]	0	82.91	0.0[b]	0	43.29	0.0[b]	1	357.43	0.0[b]
Testis	1	0.24	4.2	2	0.61	3.3	0	0.25	0.0	0	0.10	0.0	3	1.19	2.5
Kidney, renal pelvis, ureter	9	6.20	1.5	18	17.43	1.0	9	7.82	1.2	4	3.65	1.1	40	35.08	1.1
Bladder, other urinary	24	20.64	1.2	76	59.18	1.3[b]	19	27.72	0.7	12	13.97	0.9	131	121.42	1.1
Melanoma of the skin	2	2.47	0.8	8	6.98	1.1	3	3.14	1.0	2	1.52	1.3	15	14.10	1.1
Eye	0	0.34	0.0	0	0.94	0.0	0	0.41	0.0	0	0.17	0.0	0	1.86	0.0
Brain, central nervous system	1	2.01	0.5	0	5.52	0.0[b]	0	2.29	0.0	1	0.97	1.0	2	10.78	0.2[b]
Thyroid gland	0	0.56	0.0	1	1.53	0.7	0	0.67	0.0	0	0.29	0.0	1	3.05	0.3
Bone	0	0.37	0.0	0	0.98	0.0	0	0.40	0.0	0	0.17	0.0	0	1.92	0.0
Connective tissue	1	1.29	0.8	3	3.65	0.8	1	1.70	0.6	0	0.85	0.0	5	7.48	0.7
Lymphatic, hematopoietic system	**14**	**17.59**	**0.8**	**57**	**50.26**	**1.1**	**19**	**23.42**	**0.8**	**22**	**11.80**	**1.9**[b]	**112**	**102.98**	**1.1**
Non-Hodgkin's lymphoma	5	5.33	0.9	13	15.20	0.9	4	6.90	0.6	6	3.42	1.8	28	30.82	0.9
Hodgkin's disease	1	1.00	1.0	2	2.70	0.7	2	1.18	1.7	0	0.50	0.0	5	5.37	0.9
Multiple myeloma	0	2.73	0.0	11	7.87	1.4	1	3.72	0.3	3	1.91	1.6	15	16.22	0.9
Leukemias	8	8.53	0.9	31	24.49	1.3	12	11.63	1.0	13	5.97	2.2[b]	64	50.58	1.3
Chronic lymphocytic	3	2.81	1.1	9	8.10	1.1	7	3.89	1.8	5	2.03	2.5	24	16.81	1.4
Acute nonlymphocytic	4	2.52	1.6	12	7.38	1.6	2	3.55	0.6	5	1.91	2.6	23	15.34	1.5

[a] ICD-O code = 185.

[b] $P < .05$.

TESTIS
MALES

TABLE 2A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the testis, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,446	0	1,446
No. who developed a second primary cancer	104	0	104
Average age at diagnosis of first cancer, yr	35	0	35
Average yr of diagnosis of first cancer	1965	0	1965
Person-yr of follow-up	12,031	0	12,031
Average follow-up, yr	8.3	0.0	8.3
Percent given radiotherapy for first cancer	58.4	0.0	58.4

[a] ICD-O code = 186.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the testis in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	94	90.4
Only the first cancer	8	7.7
Only the second cancer	2	1.9
Neither first nor second cancer	0	0.0
Total second primary cancers	104	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

TESTIS
MALES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the testis among males in Connecticut, 1935-82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	1,446			1,189			725			451			1,446		
Person-yr in interval	1,091			3,590			2,867			4,483			12,031		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**6**	**2.04**	**2.9**[b]	**14**	**7.71**	**1.8**	**19**	**9.07**	**2.1**[b]	**65**	**31.24**	**2.1**[b]	**104**	**50.05**	**2.1**[b]
All excluding site of initial cancer	**6**	**1.98**	**3.0**[b]	**12**	**7.52**	**1.6**	**16**	**8.93**	**1.8**[b]	**64**	**31.09**	**2.1**[b]	**98**	**49.51**	**2.0**[b]
Buccal cavity, pharynx	**0**	**0.13**	**0.0**	**1**	**0.50**	**2.0**	**0**	**0.59**	**0.0**	**3**	**1.81**	**1.7**	**4**	**3.03**	**1.3**
Lip	0	0.02	0.0	1	0.08	12.3	0	0.09	0.0	0	0.23	0.0	1	0.42	2.4
Tongue	0	0.03	0.0	0	0.10	0.0	0	0.12	0.0	0	0.37	0.0	0	0.62	0.0
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.09	0.0	0	0.16	0.0
Gum, other mouth	0	0.03	0.0	0	0.14	0.0	0	0.17	0.0	2	0.55	3.7	2	0.88	2.3
Pharynx	0	0.03	0.0	0	0.13	0.0	0	0.16	0.0	0	0.51	0.0	0	0.84	0.0
Digestive system	**3**	**0.57**	**5.2**[b]	**1**	**2.16**	**0.5**	**7**	**2.59**	**2.7**[b]	**18**	**8.97**	**2.0**[b]	**29**	**14.29**	**2.0**[b]
Esophagus	0	0.04	0.0	0	0.17	0.0	1	0.20	4.9	0	0.67	0.0	1	1.08	0.9
Stomach	0	0.11	0.0	0	0.41	0.0	0	0.47	0.0	4	1.39	2.9	4	2.38	1.7
Colon	2	0.19	10.3[b]	0	0.73	0.0	3	0.89	3.4	4	3.34	1.2	9	5.15	1.7
Rectum	0	0.12	0.0	0	0.47	0.0	0	0.57	0.0	5	1.98	2.5	5	3.15	1.6
Liver, biliary	1	0.03	36.5	1	0.10	9.6	0	0.13	0.0	1	0.46	2.2	3	0.72	4.2
Pancreas	0	0.06	0.0	0	0.23	0.0	3	0.27	10.9[b]	3	0.97	3.1	6	1.53	3.9[b]
Respiratory system	**0**	**0.42**	**0.0**	**4**	**1.67**	**2.4**	**4**	**2.09**	**1.9**	**9**	**7.64**	**1.2**	**17**	**11.82**	**1.4**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0	0	0.12	0.0
Larynx	0	0.06	0.0	0	0.23	0.0	0	0.28	0.0	0	0.93	0.0	0	1.50	0.0
Trachea, bronchus, lung	0	0.35	0.0	4	1.40	2.9	4	1.77	2.3	9	6.57	1.4	17	10.08	1.7
Prostate gland	0	0.19	0.0	1	0.67	1.5	0	0.87	0.0	11	4.13	2.7[b]	12	5.86	2.0[b]
Testis	0	0.06	0.0	2	0.19	10.4[b]	3	0.14	22.1[b]	1	0.15	6.6	6	0.54	11.2[b]
Kidney, renal pelvis, ureter	0	0.06	0.0	1	0.24	4.2	0	0.29	0.0	4	0.94	4.2[b]	5	1.53	3.3[b]
Bladder, other urinary	0	0.13	0.0	1	0.49	2.1	1	0.59	1.7	7	2.23	3.1[b]	9	3.44	2.6[b]
Melanoma of the skin	1	0.06	16.2	0	0.24	0.0	0	0.25	0.0	2	0.62	3.2	3	1.17	2.6
Eye	0	0.00	0.0	0	0.02	0.0	0	0.02	0.0	0	0.05	0.0	0	0.10	0.0
Brain, central nervous system	0	0.06	0.0	0	0.21	0.0	0	0.22	0.0	0	0.55	0.0	0	1.04	0.0
Thyroid gland	0	0.02	0.0	0	0.07	0.0	0	0.07	0.0	0	0.14	0.0	0	0.30	0.0
Bone	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.05	0.0	0	0.11	0.0
Connective tissue	0	0.02	0.0	0	0.08	0.0	1	0.07	13.4	2	0.18	11.2[b]	3	0.35	8.6[b]
Lymphatic, hematopoietic system	**2**	**0.22**	**9.3**[b]	**3**	**0.78**	**3.9**	**2**	**0.80**	**2.5**	**7**	**2.32**	**3.0**[b]	**14**	**4.11**	**3.4**[b]
Non-Hodgkin's lymphoma	2	0.07	28.3[b]	1	0.27	3.8	1	0.29	3.4	2	0.85	2.4	6	1.48	4.1[b]
Hodgkin's disease	0	0.05	0.0	0	0.17	0.0	0	0.13	0.0	0	0.23	0.0	0	0.59	0.0
Multiple myeloma	0	0.02	0.0	0	0.07	0.0	0	0.09	0.0	0	0.33	0.0	0	0.51	0.0
Leukemias	0	0.07	0.0	2	0.27	7.5	1	0.29	3.5	5	0.91	5.5[b]	8	1.53	5.2[b]
Chronic lymphocytic	0	0.02	0.0	0	0.06	0.0	0	0.07	0.0	1	0.29	3.5	1	0.44	2.3
Acute nonlymphocytic	0	0.02	0.0	2	0.09	23.4[b]	0	0.09	0.0	3	0.29	10.2[b]	5	0.49	10.1[b]

[a] ICD-O code = 186.

[b] $P < .05$.

TESTIS
MALES
RADIOTHERAPY

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the testis among males given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	844			714			473			309			844		
Person-yr in interval	645			2,279			1,938			3,029			7,892		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**1.21**	**1.7**	**8**	**5.01**	**1.6**	**14**	**6.30**	**2.2**[b]	**46**	**20.87**	**2.2**[b]	**70**	**33.38**	**2.1**[b]
All excluding site of initial cancer	**2**	**1.18**	**1.7**	**8**	**4.89**	**1.6**	**12**	**6.21**	**1.9**	**45**	**20.77**	**2.2**[b]	**67**	**33.03**	**2.0**[b]
Buccal cavity, pharynx	**0**	**0.08**	**0.0**	**1**	**0.34**	**2.9**	**0**	**0.42**	**0.0**	**3**	**1.22**	**2.5**	**4**	**2.06**	**1.9**
Lip	0	0.01	0.0	1	0.05	19.1	0	0.06	0.0	0	0.15	0.0	1	0.27	3.7
Tongue	0	0.02	0.0	0	0.07	0.0	0	0.08	0.0	0	0.25	0.0	0	0.42	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.06	0.0	0	0.11	0.0
Gum, other mouth	0	0.02	0.0	0	0.09	0.0	0	0.12	0.0	2	0.37	5.4	2	0.61	3.3
Pharynx	0	0.02	0.0	0	0.09	0.0	0	0.11	0.0	0	0.35	0.0	0	0.58	0.0
Digestive system	**0**	**0.34**	**0.0**	**1**	**1.39**	**0.7**	**5**	**1.77**	**2.8**	**11**	**5.94**	**1.9**	**17**	**9.43**	**1.8**[b]
Esophagus	0	0.03	0.0	0	0.11	0.0	1	0.14	7.0	0	0.44	0.0	1	0.72	1.4
Stomach	0	0.06	0.0	0	0.26	0.0	0	0.31	0.0	3	0.91	3.3	3	1.54	1.9
Colon	0	0.11	0.0	0	0.46	0.0	2	0.61	3.3	2	2.21	0.9	4	3.39	1.2
Rectum	0	0.07	0.0	0	0.31	0.0	0	0.39	0.0	3	1.32	2.3	3	2.10	1.4
Liver, biliary	0	0.02	0.0	1	0.07	15.0	0	0.09	0.0	1	0.30	3.3	2	0.47	4.2
Pancreas	0	0.04	0.0	0	0.15	0.0	2	0.19	10.5[b]	2	0.64	3.1	4	1.02	3.9[b]
Respiratory system	**0**	**0.26**	**0.0**	**3**	**1.13**	**2.7**	**4**	**1.50**	**2.7**	**8**	**5.17**	**1.5**	**15**	**8.07**	**1.9**[b]
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0	0	0.08	0.0
Larynx	0	0.04	0.0	0	0.16	0.0	0	0.20	0.0	0	0.64	0.0	0	1.03	0.0
Trachea, bronchus, lung	0	0.22	0.0	3	0.94	3.2	4	1.27	3.2	8	4.44	1.8	15	6.87	2.2[b]
Prostate gland	0	0.10	0.0	0	0.38	0.0	0	0.57	0.0	6	2.69	2.2	6	3.74	1.6
Testis	0	0.03	0.0	0	0.12	0.0	2	0.09	21.9[b]	1	0.10	9.9	3	0.35	8.6[b]
Kidney, renal pelvis, ureter	0	0.04	0.0	1	0.16	6.2	0	0.21	0.0	3	0.64	4.7	4	1.05	3.8[b]
Bladder, other urinary	0	0.07	0.0	1	0.31	3.2	1	0.42	2.4	6	1.49	4.0[b]	8	2.30	3.5[b]
Melanoma of the skin	1	0.04	25.7	0	0.16	0.0	0	0.18	0.0	2	0.43	4.7	3	0.81	3.7
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0	0	0.07	0.0
Brain, central nervous system	0	0.04	0.0	0	0.14	0.0	0	0.16	0.0	0	0.38	0.0	0	0.71	0.0
Thyroid gland	0	0.01	0.0	0	0.05	0.0	0	0.05	0.0	0	0.10	0.0	0	0.20	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.07	0.0
Connective tissue	0	0.01	0.0	0	0.05	0.0	0	0.05	0.0	1	0.12	8.3	1	0.23	4.3
Lymphatic, hematopoietic system	**1**	**0.13**	**7.9**	**1**	**0.50**	**2.0**	**1**	**0.55**	**1.8**	**4**	**1.56**	**2.6**	**7**	**2.73**	**2.6**[b]
Non-Hodgkin's lymphoma	1	0.04	23.1	0	0.18	0.0	1	0.20	4.9	1	0.58	1.7	3	1.00	3.0
Hodgkin's disease	0	0.03	0.0	0	0.11	0.0	0	0.09	0.0	0	0.15	0.0	0	0.38	0.0
Multiple myeloma	0	0.01	0.0	0	0.05	0.0	0	0.06	0.0	0	0.22	0.0	0	0.34	0.0
Leukemias	0	0.04	0.0	1	0.17	6.0	0	0.19	0.0	3	0.60	5.0[b]	4	1.00	4.0[b]
Chronic lymphocytic	0	0.01	0.0	0	0.04	0.0	0	0.05	0.0	1	0.19	5.2	1	0.29	3.5
Acute nonlymphocytic	0	0.01	0.0	1	0.05	18.6	0	0.06	0.0	1	0.19	5.2	2	0.32	6.2

[a] ICD-O code = 186.

[b] $P < .05$.

TESTIS
MALES
NO RADIOTHERAPY

TABLE 2E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the testis among males not given radiotherapy in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	602			475			252			142			602		
Person-yr in interval	446			1,311			929			1,454			4,139		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**0.83**	**4.8^b**	**6**	**2.70**	**2.2**	**5**	**2.77**	**1.8**	**19**	**10.37**	**1.8^b**	**34**	**16.67**	**2.0^b**
All excluding site of initial cancer	**4**	**0.81**	**4.9^b**	**4**	**2.63**	**1.5**	**4**	**2.73**	**1.5**	**19**	**10.32**	**1.8^b**	**31**	**16.48**	**1.9^b**
Buccal cavity, pharynx	**0**	**0.05**	**0.0**	**0**	**0.16**	**0.0**	**0**	**0.18**	**0.0**	**0**	**0.59**	**0.0**	**0**	**0.97**	**0.0**
Lip	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.08	0.0	0	0.15	0.0
Tongue	0	0.01	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0	0	0.20	0.0
Salivary gland	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0	0	0.05	0.0
Gum, other mouth	0	0.01	0.0	0	0.04	0.0	0	0.05	0.0	0	0.17	0.0	0	0.28	0.0
Pharynx	0	0.01	0.0	0	0.04	0.0	0	0.05	0.0	0	0.16	0.0	0	0.26	0.0
Digestive system	**3**	**0.24**	**12.6^b**	**0**	**0.77**	**0.0**	**2**	**0.82**	**2.4**	**7**	**3.03**	**2.3**	**12**	**4.86**	**2.5^b**
Esophagus	0	0.02	0.0	0	0.06	0.0	0	0.06	0.0	0	0.22	0.0	0	0.36	0.0
Stomach	0	0.05	0.0	0	0.15	0.0	0	0.16	0.0	1	0.48	2.1	1	0.84	1.2
Colon	2	0.08	24.6^b	0	0.27	0.0	1	0.28	3.6	2	1.13	1.8	5	1.76	2.8
Rectum	0	0.05	0.0	0	0.16	0.0	0	0.18	0.0	2	0.66	3.0	2	1.05	1.9
Liver, biliary	1	0.01	86.9^b	0	0.04	0.0	0	0.04	0.0	0	0.15	0.0	1	0.24	4.1
Pancreas	0	0.02	0.0	0	0.08	0.0	1	0.08	11.9	1	0.33	3.0	2	0.51	3.9
Respiratory system	**0**	**0.16**	**0.0**	**1**	**0.54**	**1.9**	**0**	**0.59**	**0.0**	**1**	**2.47**	**0.4**	**2**	**3.75**	**0.5**
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Larynx	0	0.02	0.0	0	0.07	0.0	0	0.08	0.0	0	0.30	0.0	0	0.46	0.0
Trachea, bronchus, lung	0	0.13	0.0	1	0.45	2.2	0	0.50	0.0	1	2.13	0.5	2	3.21	0.6
Prostate gland	0	0.09	0.0	1	0.29	3.5	0	0.30	0.0	5	1.44	3.5^b	6	2.12	2.8^b
Testis	0	0.02	0.0	2	0.07	28.0^b	1	0.04	22.3	0	0.05	0.0	3	0.19	15.7^b
Kidney, renal pelvis, ureter	0	0.02	0.0	0	0.08	0.0	0	0.08	0.0	1	0.30	3.3	1	0.49	2.1
Bladder, other urinary	0	0.05	0.0	0	0.17	0.0	0	0.18	0.0	1	0.74	1.4	1	1.14	0.9
Melanoma of the skin	0	0.02	0.0	0	0.08	0.0	0	0.07	0.0	0	0.19	0.0	0	0.36	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.03	0.0
Brain, central nervous system	0	0.02	0.0	0	0.07	0.0	0	0.06	0.0	0	0.17	0.0	0	0.33	0.0
Thyroid gland	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.05	0.0	0	0.09	0.0
Bone	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	1	0.02	42.5	1	0.06	17.0	2	0.12	17.2^b
Lymphatic, hematopoietic system	**1**	**0.09**	**11.3**	**2**	**0.28**	**7.2**	**1**	**0.25**	**4.0**	**3**	**0.77**	**3.9**	**7**	**1.38**	**5.1^b**
Non-Hodgkin's lymphoma	1	0.03	36.7	1	0.09	11.3	0	0.09	0.0	1	0.27	3.7	3	0.47	6.4^b
Hodgkin's disease	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.08	0.0	0	0.21	0.0
Multiple myeloma	0	0.01	0.0	0	0.02	0.0	0	0.03	0.0	0	0.11	0.0	0	0.17	0.0
Leukemias	0	0.03	0.0	1	0.10	10.1	1	0.09	10.8	2	0.31	6.5	4	0.53	7.5^b
Chronic lymphocytic	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0	0	0.15	0.0
Acute nonlymphocytic	0	0.01	0.0	1	0.03	31.5	0	0.03	0.0	2	0.10	20.1^b	3	0.17	17.6^b

[a] ICD-O code = 186.

[b] $P < .05$.

Second Cancer Following Cancer of the Urinary System in Connecticut, 1935–82 [1]

Arlene F. Kantor *and* Joseph K. McLaughlin [2]

ABSTRACT—The risk of second primary cancer was assessed in persons who developed cancer of the urinary tract in Connecticut during 1935-82. Among 12,384 patients with a first primary tumor of the bladder or urethra, a second cancer was reported in 1,151 (or 9%). A significantly elevated relative risk (RR) of 1.23 was due to excess cancers of the lung, larynx, prostate, and kidney, and acute nonlymphocytic leukemia. Among 5,115 persons with a first primary tumor of the kidney, renal pelvis or ureter, a second cancer was reported in 374 (or 7%) that yielded a significantly elevated RR of 1.54 due to excess tumors of the bladder and prostate and second primary kidney neoplasms. The role of common etiologic factors, such as cigarette smoking, the multifocal tendency of tumors of the urinary tract, and heightened medical surveillance are discussed in relation to these findings.—Natl Cancer Inst Monogr 68: 149-159, 1985.

Urinary tract cancer accounts for nearly 10% of all tumors in men and 4% in women (*1*). Cancers of the urinary bladder account for two-thirds of all urinary tract neoplasms. Approximately 85% of other urinary tract tumors arise in the renal parenchyma (renal cell carcinoma). The remaining tumors are primarily renal pelvis and ureter neoplasms, which share epidemiologic characteristics with bladder cancer and are histologically similar (mainly transitional cell carcinomas). A small proportion of kidney neoplasms consists of Wilms' tumor (nephroblastoma), which arises in childhood.

URINARY BLADDER (ICD-O, 188, 189.3–189.9)

Cancers of the urinary bladder including the urethra account for 7% of all cancers among males and less than 3% among females (*1*). The relative 5-year survival is 60% (*2*), with most tumors confined to the bladder mucosa or submucosa at diagnosis (*3*). Most patients (75%) are treated initially with surgery alone, with a small proportion given radiotherapy or chemotherapy (*4*).

Epidemiologic studies have linked the risk of bladder cancer to cigarette smoking (*5, 6*), occupational exposures in the dyestuffs, rubber, leather, and painting industries (*7, 8*), abuse of analgesics containing phenacetin (*9*), urinary tract infection (*3, 10*), and pelvic radiation for gynecologic disorders (*11, 12*). Associations with artificial sweeteners (*13, 14*) and coffee drinking (*15, 16*) have been suspected but not confirmed.

A previous study of second neoplasms following bladder cancer in Connecticut revealed increased risks for tumors of the kidney, prostate, lung, and tongue (*17*). Earlier studies have also shown a tendency toward multifocal tumors involving the transitional epithelial surfaces of the urinary tract, i.e., bladder, renal pelvis, and ureter (*18*).

Results

A total of 12,384 persons were reported to the Connecticut Tumor Registry with a first primary neoplasm of the bladder during the period 1935–82 and were followed for a total of 61,113 person-years. The average age at diagnosis of the first tumor was 66 years, and average follow-up was 4.9 years. Most of the patients were male (74%). Radiation therapy was initially given to 21% of the patients.

Overall, 1,151 patients (or 9%) developed a second primary neoplasm, compared with 937 expected based on incidence rates in the general population (RR = 1.23; 95% CI = 1.16–1.30). A significant excess occurred among men (RR = 1.3) and a lower nonsignificant excess in women (RR = 1.1). Significant increases were observed for cancers of the larynx (RR = 1.7), lung (RR = 1.5), prostate (RR = 1.6), and kidney (RR = 4.6). Significant increases were observed for ANLL, non-Hodgkin's lymphoma, and bone cancer in men. Approximately 75% of second tumors of the kidney arose in the renal pelvis or ureter.

The risk of second cancer was significantly elevated in each follow-up period and was highest in the first year after diagnosis of the index primary tumor. Some site-specific patterns differed from this overall trend. The risk of non-Hodgkin's lymphoma appeared to increase over time and was limited to the group of 2,612 patients who received radiation therapy. The risks of prostate and kidney cancers declined after the first year of follow-up but remained elevated. A significant increase in female breast cancer was limited to the first year of follow-up.

Among 2,017 persons observed for 10 or more years after the initial diagnosis of bladder cancer, 237 (or 12%) developed second primary neoplasms versus 198 expected (RR = 1.2; 95% CI = 1.1–1.4), with tumors of the lung predominating. A significant excess of kidney cancer was observed in both sexes, as well as thyroid cancer and non-Hodgkin's lymphoma in men.

ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Environmental Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3C07, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Arlene F. Kantor, Dr. P.H.

The overall RR of second cancer was slightly higher in patients who received radiation as initial therapy (1.4; 95% CI = 1.2–1.7), compared with those who did not (1.2; 95% CI = 1.1–1.3). Significant excesses of cancer of the tongue (RR = 4.2) and non-Hodgkin's lymphoma (RR = 3.2) were noted among patients receiving radiation therapy; nonsignificant excesses for these tumors were also seen among patients who did not receive radiation therapy. The risks of lung, prostate, and kidney cancers were slightly higher among patients given radiation treatment when compared with the risks among those who did not.

A significant deficit of second bladder cancer was observed, which is related to cystectomy for some bladder tumors and to registry practices which do not require the reporting of second transitional cell carcinomas of the bladder. When the observed and expected numbers of second bladder tumors are excluded from analysis, the overall RR of other tumors would be 1.29 (95% CI = 1.2–1.4). Further exclusion of second tumors of the prostate would yield an overall RR of 1.23 (95% CI = 1.2–1.3).

Discussion

Our analyses indicate that patients with a first primary tumor of the bladder were at a significant 23% increased risk of developing a second primary cancer. A significantly high risk of lung and laryngeal tumors appeared consistent with the effect of cigarette smoking. An excess of prostate tumors, particularly in the first year of follow-up, may be due to increased medical surveillance and higher autopsy rates among cancer patients when compared with the general population. The increased risk of second tumors of the kidney, renal pelvis, and ureter may be explained by common risk factors and the multicentricity of transitional cell tumors involving the urinary tract. The significant excess of ANLL is due partly to the higher risk of this tumor observed among patients given radiation therapy, but it may also be related to treatment with alkylating agents which have been associated with leukemia risk in other groups of cancer patients (*4, 19*).

The overall risk of second cancer was significantly elevated throughout all years of follow-up but was highest in the first year (1.6). Risk of non-Hodgkin's lymphoma, which increased with years of follow-up and was limited to male patients who received radiation therapy, is notable because some reports have suggested an increased risk of this tumor among persons exposed to atomic bomb or therapeutic radiation (*20, 21*), but the evidence for this association is not consistent (*22*).

KIDNEY, RENAL PELVIS, AND URETER (ICD-O, 189.0–189.2)

Cancers of the kidney, including renal pelvis and ureter, account for nearly 3% of all cancers among males and less than 2% among females (*1*). Relative survival now approaches 50% (*2*) with approximately one-half the patients diagnosed with localized disease (*23*). Most (61%) are initially treated with surgery alone (*4*).

A limited number of risk factors have been identified in epidemiologic studies of kidney cancer. Cigarette smoking has been reported in several studies as a moderate risk factor for renal cell carcinoma (*24–27*), whereas cancer of the renal pelvis, which shares epidemiologic characteristics with bladder cancer (*28*), is strongly associated with past cigarette use (*29*). An association with heavy analgesic intake has been reported (*26, 29*), particularly between phenacetin-containing compounds and tumors of the renal pelvis and ureter (*30*). A relationship between high relative weight and renal cell carcinoma in women has been seen in several studies (*25–27*).

An earlier Connecticut study of second primary neoplasms following kidney cancer identified significant excesses of prostate and bladder tumors (*17*). A twofold risk of leukemia following renal cancer has also been identified that seemed unrelated to initial treatment (*4*). However, second cancers resulting from radiotherapy for Wilms' tumor in childhood have been reported (*31*).

Results

A total of 5,115 persons with primary cancer of the kidney were reported to the Connecticut Tumor Registry during the period 1935–82 and were followed for a total of 22,059 person-years. The average age at diagnosis of the index tumor was 59 years, and average follow-up was 4.3 years. Radiation therapy was initially given to 21% of these patients.

A second primary neoplasm was reported in 374 patients (or 7%), compared with 243 expected based on incidence rates in the general population (RR = 1.54; 95% CI = 1.39–1.71). The risk of second cancer was significantly high in both sexes. Significantly increased risks were observed for tumors arising in the bladder (RR = 6.9; n = 99), kidney (RR = 2.9; n = 16), prostate (RR = 1.5; n = 43), and bone (RR = 9.0; n = 3). Approximately 85% of the patients with second primary tumors arising in the urinary tract had index neoplasms of the renal pelvis or ureter. The 16 persons with second kidney cancer included 9 with bilateral renal cancer, 2 with cancer of the ureter followed by kidney cancer, and 5 with cancer of the renal pelvis or ureter who developed a second cancer of the renal pelvis or ureter. Excesses of borderline statistical significance were seen for lymphatic and hematopoietic neoplasms (RR = 1.5; n = 25) and lung cancer (RR = 1.3; n = 47).

The risk of second tumors following kidney cancer was significantly elevated in the first 5 years of follow-up and to a lesser degree in persons followed 10 years or longer. A decrease in risk over time was observed for second tumors of the bladder and kidney. Risk of prostate cancer was not consistently associated with length of follow-up.

Among 717 persons with renal neoplasms who were followed at least 10 years, a significant 41% excess of second tumors was found (84 cases observed vs. 59.8 expected). This was due to a significant increase in prostate cancer and nonsignificant excesses of bladder cancer and digestive tract cancers, mainly of the rectum and pancreas. However, 9 of the 42 second prostate cancers were reported at autopsy or on death certificates, and if they are removed from the analysis, the excess is reduced to 25%.

Among 1,066 persons who received radiation therapy, a significant 57% excess of second primary neoplasms was observed (29 vs. 18.5), similar to the excess seen among patients who did not receive this treatment. A significant excess of malignant melanoma was observed among patients treated with radiation (RR = 11), but the RR was based on only 2 cases.

Discussion

A significant 54% increase in the risk of second primary tumors was observed following kidney cancer, due mainly to excesses of genitourinary neoplasms and lung cancer. The greatly increased risk of bladder cancer following kidney cancer may result from the multifocal nature of transitional epithelial tumors of the lower urinary tract or shared risk factors (e.g., cigarette smoking), particularly for index tumors of the renal pelvis and ureter (*32*). The significant excess of second kidney tumors also reflects the tendency to multicentric neoplasms of the lower urinary tract, although misdiagnosis of metastases may occur occasionally. An excess of prostate cancer is at least partly due to increased medical surveillance of cancer patients, compared with the general population. The excess of bone cancer was based on only 3 cases and may be due to metastatic disease or to radiation-induced sarcomas, although 2 of the bone cancers were recorded solely on the basis of death certificate information and therefore were not histologically confirmed. A nonsignificant increase in lung cancer following kidney cancer may be related to the impact of cigarette smoking on both tumors, but evaluation of the potential problem of pulmonary metastases is difficult with the present data.

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KIDNEY
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the kidney, renal pelvis, or ureter, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	3,284	1,831	5,115
No. who developed a second primary cancer	261	113	374
Average age at diagnosis of first cancer, yr	59	59	59
Average yr of diagnosis of first cancer	1966	1966	1966
Person-yr of follow-up	13,336	8,723	22,059
Average follow-up, yr	4.1	4.8	4.3
Percent given radiotherapy for first cancer	21.3	20.0	20.8

[a] ICD-O codes = 189.0–189.2.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the kidney, renal pelvis, or ureter in Connecticut, 1935-82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	329	88.0
Only the first cancer	42	11.2
Only the second cancer	2	0.5
Neither first nor second cancer	1	0.3
Total second primary cancers	374	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

KIDNEY
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the kidney, renal pelvis, or ureter among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,115			3,311			1,494			717			5,115		
Person-yr in interval	3,301			8,654			5,228			4,877			22,059		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**64**	**34.10**	**1.9**[b]	**159**	**91.59**	**1.7**[b]	**67**	**57.34**	**1.2**	**84**	**59.78**	**1.4**[b]	**374**	**242.65**	**1.5**[b]
All excluding site of initial cancer	**61**	**33.30**	**1.8**[b]	**152**	**89.47**	**1.7**[b]	**63**	**56.03**	**1.1**	**82**	**58.49**	**1.4**[b]	**358**	**237.13**	**1.5**[b]
Buccal cavity, pharynx	**0**	**1.43**	**0.0**	**4**	**3.75**	**1.1**	**2**	**2.24**	**0.9**	**2**	**2.10**	**1.0**	**8**	**9.51**	**0.8**
Lip	0	0.22	0.0	2	0.56	3.5	1	0.32	3.1	0	0.30	0.0	3	1.40	2.1
Tongue	0	0.29	0.0	0	0.75	0.0	1	0.45	2.2	1	0.41	2.4	2	1.90	1.1
Salivary gland	0	0.08	0.0	0	0.22	0.0	0	0.14	0.0	0	0.15	0.0	0	0.59	0.0
Gum, other mouth	0	0.42	0.0	1	1.10	0.9	0	0.67	0.0	0	0.63	0.0	1	2.81	0.4
Pharynx	0	0.36	0.0	1	0.96	1.0	0	0.58	0.0	1	0.53	1.9	2	2.43	0.8
Digestive system	**8**	**10.66**	**0.8**	**25**	**28.40**	**0.9**	**14**	**17.64**	**0.8**	**26**	**18.53**	**1.4**	**73**	**75.18**	**1.0**
Esophagus	0	0.59	0.0	0	1.55	0.0	0	0.92	0.0	0	0.87	0.0	0	3.93	0.0[b]
Stomach	2	1.75	1.1	4	4.48	0.9	3	2.67	1.1	4	2.66	1.5	13	11.55	1.1
Colon	3	4.26	0.7	15	11.52	1.3	7	7.30	1.0	8	8.01	1.0	33	31.07	1.1
Rectum	0	2.19	0.0	5	5.84	0.9	4	3.62	1.1	8	3.69	2.2	17	15.33	1.1
Liver, biliary	0	0.59	0.0	0	1.59	0.0	0	0.99	0.0	2	1.06	1.9	2	4.23	0.5
Pancreas	3	1.09	2.8	1	2.92	0.3	0	1.83	0.0	4	1.92	2.1	8	7.76	1.0
Respiratory system	**5**	**5.76**	**0.9**	**22**	**15.49**	**1.4**	**13**	**9.63**	**1.4**	**11**	**9.51**	**1.2**	**51**	**40.36**	**1.3**
Nasal cavities, sinuses	0	0.07	0.0	0	0.18	0.0	0	0.11	0.0	0	0.11	0.0	0	0.47	0.0
Larynx	0	0.63	0.0	3	1.65	1.8	0	1.00	0.0	0	0.90	0.0	3	4.17	0.7
Trachea, bronchus, lung	4	5.01	0.8	19	13.51	1.4	13	8.42	1.5	11	8.41	1.3	47	35.34	1.3
Female breast	3	2.60	1.2	8	7.13	1.1	6	4.74	1.3	6	5.18	1.2	23	19.64	1.2
Female genital tract	**3**	**1.65**	**1.8**	**2**	**4.44**	**0.5**	**3**	**2.90**	**1.0**	**2**	**3.00**	**0.7**	**10**	**11.98**	**0.8**
Cervix uteri	1	0.32	3.2	1	0.82	1.2	1	0.51	2.0	0	0.48	0.0	3	2.12	1.4
Corpus uteri	1	0.68	1.5	1	1.87	0.5	1	1.26	0.8	1	1.33	0.8	4	5.13	0.8
Uterus, NOS	1	0.11	8.9	0	0.27	0.0	1	0.16	6.2	0	0.16	0.0	2	0.70	2.8
Ovary, fallopian tubes	0	0.45	0.0	0	1.22	0.0	0	0.80	0.0	1	0.83	1.2	1	3.30	0.3
Prostate gland	9	4.04	2.2[b]	13	11.03	1.2	5	6.89	0.7	16	7.58	2.1[b]	43	29.53	1.5[b]
Testis	1	0.05	20.6	0	0.12	0.0	0	0.06	0.0	0	0.06	0.0	1	0.30	3.4
Kidney, renal pelvis, ureter	3	0.80	3.7	7	2.12	3.3[b]	4	1.31	3.1	2	1.29	1.5	16	5.52	2.9[b]
Bladder, other urinary	24	2.00	12.0[b]	57	5.40	10.6[b]	10	3.37	3.0[b]	8	3.60	2.2	99	14.35	6.9[b]
Melanoma of the skin	0	0.40	0.0	0	1.10	0.0	1	0.69	1.5	2	0.68	2.9	3	2.88	1.0
Eye	0	0.05	0.0	0	0.14	0.0	0	0.09	0.0	0	0.08	0.0	0	0.37	0.0
Brain, central nervous system	2	0.39	5.1	1	1.04	1.0	0	0.64	0.0	1	0.59	1.7	4	2.67	1.5
Thyroid gland	0	0.14	0.0	1	0.38	2.6	0	0.24	0.0	0	0.24	0.0	1	0.99	1.0
Bone	0	0.05	0.0	2	0.13	15.6[b]	0	0.08	0.0	1	0.08	12.9	3	0.33	9.0[b]
Connective tissue	2	0.16	12.3[b]	1	0.43	2.3	0	0.27	0.0	0	0.27	0.0	3	1.13	2.6
Lymphatic, hematopoietic system	**3**	**2.26**	**1.3**	**11**	**6.12**	**1.8**	**7**	**3.85**	**1.8**	**4**	**4.10**	**1.0**	**25**	**16.32**	**1.5**
Non-Hodgkin's lymphoma	0	0.78	0.0	4	2.12	1.9	4	1.34	3.0	2	1.40	1.4	10	5.63	1.8
Hodgkin's disease	0	0.17	0.0	0	0.44	0.0	0	0.27	0.0	0	0.27	0.0	0	1.14	0.0
Multiple myeloma	2	0.36	5.6	1	0.98	1.0	1	0.63	1.6	1	0.69	1.4	5	2.65	1.9
Leukemias	1	0.95	1.1	6	2.58	2.3	2	1.61	1.2	1	1.74	0.6	10	6.89	1.5
Chronic lymphocytic	0	0.29	0.0	2	0.81	2.5	1	0.51	2.0	1	0.57	1.8	4	2.17	1.8
Acute nonlymphocytic	1	0.29	3.4	2	0.81	2.5	0	0.51	0.0	0	0.57	0.0	3	2.18	1.4

[a] ICD-O codes = 189.0–189.2.

[b] $P < .05$.

KIDNEY
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the kidney, renal pelvis, or ureter among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,284			2,105			913			410			3,284		
Person-yr in interval	2,104			5,412			3,106			2,714			13,336		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**45**	**23.95**	**1.9**[b]	**113**	**63.78**	**1.8**[b]	**49**	**38.82**	**1.3**	**54**	**38.86**	**1.4**[b]	**261**	**165.30**	**1.6**[b]
All excluding site of initial cancer	**43**	**23.32**	**1.8**[b]	**108**	**62.11**	**1.7**[b]	**48**	**37.81**	**1.3**	**53**	**37.90**	**1.4**[b]	**252**	**161.03**	**1.6**[b]
Buccal cavity, pharynx	**0**	**1.25**	**0.0**	**4**	**3.26**	**1.2**	**2**	**1.91**	**1.0**	**2**	**1.73**	**1.2**	**8**	**8.15**	**1.0**
Lip	0	0.21	0.0	2	0.54	3.7	1	0.30	3.3	0	0.27	0.0	3	1.32	2.3
Tongue	0	0.25	0.0	0	0.65	0.0	1	0.38	2.6	1	0.34	3.0	2	1.62	1.2
Salivary gland	0	0.06	0.0	0	0.16	0.0	0	0.10	0.0	0	0.10	0.0	0	0.42	0.0
Gum, other mouth	0	0.35	0.0	1	0.93	1.1	0	0.55	0.0	0	0.49	0.0	1	2.33	0.4
Pharynx	0	0.32	0.0	1	0.85	1.2	0	0.50	0.0	1	0.45	2.2	2	2.12	0.9
Digestive system	**5**	**7.54**	**0.7**	**18**	**19.87**	**0.9**	**12**	**11.95**	**1.0**	**13**	**11.80**	**1.1**	**48**	**51.12**	**0.9**
Esophagus	0	0.52	0.0	0	1.36	0.0	0	0.79	0.0	0	0.73	0.0	0	3.39	0.0
Stomach	2	1.35	1.5	4	3.43	1.2	2	2.00	1.0	2	1.87	1.1	10	8.65	1.2
Colon	1	2.79	0.4	10	7.46	1.3	6	4.57	1.3	5	4.74	1.1	22	19.55	1.1
Rectum	0	1.60	0.0	3	4.21	0.7	4	2.53	1.6	4	2.43	1.6	11	10.76	1.0
Liver, biliary	0	0.38	0.0	0	1.02	0.0	0	0.62	0.0	0	0.62	0.0	0	2.63	0.0
Pancreas	2	0.77	2.6	1	2.05	0.5	0	1.24	0.0	2	1.22	1.6	5	5.28	0.9
Respiratory system	**5**	**5.12**	**1.0**	**16**	**13.68**	**1.2**	**12**	**8.39**	**1.4**	**8**	**8.09**	**1.0**	**41**	**35.26**	**1.2**
Nasal cavities, sinuses	0	0.05	0.0	0	0.14	0.0	0	0.08	0.0	0	0.08	0.0	0	0.35	0.0
Larynx	0	0.59	0.0	3	1.55	1.9	0	0.93	0.0	0	0.82	0.0	3	3.89	0.8
Trachea, bronchus, lung	4	4.43	0.9	13	11.88	1.1	12	7.30	1.6	8	7.12	1.1	37	30.71	1.2
Prostate gland	9	4.04	2.2[b]	13	11.03	1.2	5	6.89	0.7	16	7.58	2.1[b]	43	29.53	1.5[b]
Testis	1	0.05	20.6	0	0.12	0.0	0	0.06	0.0	0	0.06	0.0	1	0.30	3.4
Kidney, renal pelvis, ureter	2	0.63	3.2	5	1.67	3.0	1	1.01	1.0	1	0.96	1.0	9	4.27	2.1
Bladder, other urinary	17	1.72	9.9[b]	42	4.61	9.1[b]	9	2.84	3.2[b]	6	2.94	2.0	74	12.10	6.1[b]
Melanoma of the skin	0	0.29	0.0	0	0.78	0.0	1	0.48	2.1	1	0.45	2.2	2	2.00	1.0
Eye	0	0.04	0.0	0	0.10	0.0	0	0.06	0.0	0	0.05	0.0	0	0.24	0.0
Brain, central nervous system	2	0.29	7.0	0	0.75	0.0	0	0.45	0.0	0	0.39	0.0	2	1.88	1.1
Thyroid gland	0	0.07	0.0	1	0.19	5.4	0	0.11	0.0	0	0.10	0.0	1	0.46	2.2
Bone	0	0.03	0.0	2	0.09	22.1[b]	0	0.05	0.0	0	0.05	0.0	2	0.23	8.8
Connective tissue	2	0.12	16.7[b]	0	0.32	0.0	0	0.19	0.0	0	0.19	0.0	2	0.81	2.5
Lymphatic, hematopoietic system	**1**	**1.60**	**0.6**	**8**	**4.27**	**1.9**	**5**	**2.60**	**1.9**	**4**	**2.63**	**1.5**	**18**	**11.09**	**1.6**
Non-Hodgkin's lymphoma	0	0.53	0.0	3	1.42	2.1	3	0.86	3.5	2	0.85	2.4	8	3.66	2.2
Hodgkin's disease	0	0.12	0.0	0	0.32	0.0	0	0.18	0.0	0	0.17	0.0	0	0.79	0.0
Multiple myeloma	0	0.24	0.0	1	0.65	1.5	1	0.40	2.5	1	0.42	2.4	3	1.71	1.8
Leukemias	1	0.70	1.4	4	1.88	2.1	1	1.15	0.9	1	1.19	0.8	7	4.92	1.4
Chronic lymphocytic	0	0.22	0.0	2	0.61	3.3	1	0.38	2.7	1	0.40	2.5	4	1.61	2.5
Acute nonlymphocytic	1	0.21	4.8	1	0.57	1.8	0	0.36	0.0	0	0.38	0.0	2	1.51	1.3

[a] ICD-O codes = 189.0–189.2.

[b] $P < .05$.

KIDNEY
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the kidney, renal pelvis, or ureter among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,831			1,206			581			307			1,831		
Person-yr in interval	1,197			3,242			2,121			2,163			8,723		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**19**	**10.15**	**1.9**[b]	**46**	**27.81**	**1.7**[b]	**18**	**18.52**	**1.0**	**30**	**20.91**	**1.4**	**113**	**77.35**	**1.5**[b]
All excluding site of initial cancer	**18**	**9.98**	**1.8**[b]	**44**	**27.36**	**1.6**[b]	**15**	**18.22**	**0.8**	**29**	**20.57**	**1.4**	**106**	**76.10**	**1.4**[b]
Buccal cavity, pharynx	**0**	**0.18**	**0.0**	**0**	**0.49**	**0.0**	**0**	**0.33**	**0.0**	**0**	**0.37**	**0.0**	**0**	**1.36**	**0.0**
Lip	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Tongue	0	0.04	0.0	0	0.10	0.0	0	0.07	0.0	0	0.07	0.0	0	0.28	0.0
Salivary gland	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.17	0.0
Gum, other mouth	0	0.06	0.0	0	0.17	0.0	0	0.12	0.0	0	0.13	0.0	0	0.48	0.0
Pharynx	0	0.04	0.0	0	0.11	0.0	0	0.07	0.0	0	0.08	0.0	0	0.30	0.0
Digestive system	**3**	**3.12**	**1.0**	**7**	**8.53**	**0.8**	**2**	**5.69**	**0.4**	**13**	**6.73**	**1.9**[b]	**25**	**24.06**	**1.0**
Esophagus	0	0.07	0.0	0	0.19	0.0	0	0.13	0.0	0	0.15	0.0	0	0.54	0.0
Stomach	0	0.40	0.0	0	1.04	0.0	1	0.67	1.5	2	0.79	2.5	3	2.91	1.0
Colon	2	1.47	1.4	5	4.06	1.2	1	2.73	0.4	3	3.27	0.9	11	11.52	1.0
Rectum	0	0.60	0.0	2	1.63	1.2	0	1.09	0.0	4	1.26	3.2	6	4.56	1.3
Liver, biliary	0	0.21	0.0	0	0.57	0.0	0	0.37	0.0	2	0.44	4.5	2	1.59	1.3
Pancreas	1	0.32	3.2	0	0.87	0.0	0	0.59	0.0	2	0.70	2.8	3	2.48	1.2
Respiratory system	**0**	**0.64**	**0.0**	**6**	**1.81**	**3.3**[b]	**1**	**1.24**	**0.8**	**3**	**1.42**	**2.1**	**10**	**5.10**	**2.0**
Nasal cavities, sinuses	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Larynx	0	0.04	0.0	0	0.10	0.0	0	0.07	0.0	0	0.08	0.0	0	0.28	0.0
Trachea, bronchus, lung	0	0.58	0.0	6	1.64	3.7[b]	1	1.12	0.9	3	1.29	2.3	10	4.63	2.2[b]
Female breast	3	2.60	1.2	8	7.13	1.1	6	4.74	1.3	6	5.18	1.2	23	19.64	1.2
Female genital tract	**3**	**1.65**	**1.8**	**2**	**4.44**	**0.5**	**3**	**2.90**	**1.0**	**2**	**3.00**	**0.7**	**10**	**11.98**	**0.8**
Cervix uteri	1	0.32	3.2	1	0.82	1.2	1	0.51	2.0	0	0.48	0.0	3	2.12	1.4
Corpus uteri	1	0.68	1.5	1	1.87	0.5	1	1.26	0.8	1	1.33	0.8	4	5.13	0.8
Uterus, NOS	1	0.11	8.9	0	0.27	0.0	1	0.16	6.2	0	0.16	0.0	2	0.70	2.8
Ovary, fallopian tubes	0	0.45	0.0	0	1.22	0.0	0	0.80	0.0	1	0.83	1.2	1	3.30	0.3
Kidney, renal pelvis, ureter	1	0.17	6.0	2	0.45	4.4	3	0.30	10.0[b]	1	0.34	3.0	7	1.25	5.6[b]
Bladder, other urinary	7	0.28	24.8[b]	15	0.79	19.1[b]	1	0.53	1.9	2	0.65	3.1	25	2.25	11.1[b]
Melanoma of the skin	0	0.11	0.0	0	0.32	0.0	0	0.21	0.0	1	0.23	4.3	1	0.88	1.1
Eye	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.04	0.0	0	0.13	0.0
Brain, central nervous system	0	0.11	0.0	1	0.29	3.4	0	0.19	0.0	1	0.20	5.1	2	0.79	2.5
Thyroid gland	0	0.07	0.0	0	0.19	0.0	0	0.13	0.0	0	0.14	0.0	0	0.53	0.0
Bone	0	0.01	0.0	0	0.04	0.0	0	0.02	0.0	1	0.03	36.0	1	0.10	9.5
Connective tissue	0	0.04	0.0	1	0.12	8.5	0	0.08	0.0	0	0.09	0.0	1	0.32	3.1
Lymphatic, hematopoietic system	**2**	**0.66**	**3.0**	**3**	**1.85**	**1.6**	**2**	**1.25**	**1.6**	**0**	**1.47**	**0.0**	**7**	**5.23**	**1.3**
Non-Hodgkin's lymphoma	0	0.25	0.0	1	0.70	1.4	1	0.47	2.1	0	0.55	0.0	2	1.97	1.0
Hodgkin's disease	0	0.05	0.0	0	0.12	0.0	0	0.08	0.0	0	0.09	0.0	0	0.35	0.0
Multiple myeloma	2	0.12	17.3[b]	0	0.33	0.0	0	0.23	0.0	0	0.27	0.0	2	0.94	2.1
Leukemias	0	0.25	0.0	2	0.70	2.9	1	0.46	2.2	0	0.56	0.0	3	1.96	1.5
Chronic lymphocytic	0	0.07	0.0	0	0.20	0.0	0	0.13	0.0	0	0.17	0.0	0	0.57	0.0
Acute nonlymphocytic	0	0.08	0.0	1	0.24	4.3	0	0.16	0.0	0	0.19	0.0	1	0.67	1.5

[a] ICD-O codes = 189.0–189.2.

[b] $P < .05$.

BLADDER
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the bladder or other urinary, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	9,139	3,245	12,384
No. who developed a second primary cancer	949	202	1,151
Average age at diagnosis of first cancer, yr	66	67	66
Average yr of diagnosis of first cancer	1967	1967	1967
Person-yr of follow-up	44,794	16,319	61,113
Average follow-up, yr	4.9	5.0	4.9
Percent given radiotherapy for first cancer	20.5	22.8	21.1

[a] ICD-O codes 188, 189.3–189.9.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the bladder or other urinary in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	1,016	88.3
Only the first cancer	117	10.2
Only the second cancer	14	1.2
Neither first nor second cancer	4	0.3
Total second primary cancers	1,151	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

BLADDER
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bladder or other urinary among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	12,384			9,357			4,535			2,017			12,384		
Person-yr in interval	8,809			25,604			15,552			11,148			61,113		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**196**	**125.99**	**1.6^b**	**427**	**373.43**	**1.1^b**	**291**	**240.56**	**1.2^b**	**237**	**197.83**	**1.2^b**	**1,151**	**937.18**	**1.2^b**
All excluding site of initial cancer	**189**	**117.72**	**1.6^b**	**416**	**348.72**	**1.2^b**	**290**	**224.55**	**1.3^b**	**234**	**184.39**	**1.3^b**	**1,129**	**874.79**	**1.3^b**
Buccal cavity, pharynx	**7**	**5.31**	**1.3**	**19**	**15.38**	**1.2**	**8**	**9.53**	**0.8**	**5**	**7.15**	**0.7**	**39**	**37.33**	**1.0**
Lip	1	0.93	1.1	2	2.59	0.8	0	1.57	0.0	2	1.19	1.7	5	6.28	0.8
Tongue	1	1.05	1.0	5	3.02	1.7	3	1.86	1.6	3	1.37	2.2	12	7.29	1.6
Salivary gland	0	0.31	0.0	1	0.92	1.1	0	0.59	0.0	0	0.48	0.0	1	2.31	0.4
Gum, other mouth	2	1.52	1.3	6	4.42	1.4	1	2.77	0.4	0	2.08	0.0	9	10.79	0.8
Pharynx	1	1.29	0.8	4	3.80	1.1	4	2.35	1.7	0	1.75	0.0	9	9.19	1.0
Digestive system	**35**	**40.59**	**0.9**	**113**	**118.54**	**1.0**	**75**	**76.19**	**1.0**	**59**	**62.80**	**0.9**	**282**	**297.91**	**0.9**
Esophagus	0	2.26	0.0	7	6.52	1.1	3	4.05	0.7	2	3.06	0.7	12	15.87	0.8
Stomach	5	6.96	0.7	14	19.51	0.7	14	12.15	1.2	12	9.59	1.3	45	48.17	0.9
Colon	13	16.18	0.8	39	48.00	0.8	29	31.45	0.9	23	26.85	0.9	104	122.40	0.8
Rectum	9	8.16	1.1	23	23.91	1.0	15	15.28	1.0	11	12.35	0.9	58	59.66	1.0
Liver, biliary	1	2.22	0.5	14	6.47	2.2^b	4	4.19	1.0	1	3.53	0.3	20	16.39	1.2
Pancreas	6	4.11	1.5	13	12.12	1.1	8	7.80	1.0	9	6.41	1.4	36	30.42	1.2
Respiratory system	**25**	**21.55**	**1.2**	**100**	**65.28**	**1.5^b**	**73**	**41.59**	**1.8^b**	**46**	**32.65**	**1.4^b**	**244**	**160.96**	**1.5^b**
Nasal cavities, sinuses	2	0.25	7.9	0	0.75	0.0	0	0.47	0.0	1	0.38	2.6	3	1.85	1.6
Larynx	3	2.26	1.3	8	6.68	1.2	13	4.13	3.1^b	4	3.02	1.3	28	16.08	1.7^b
Trachea, bronchus, lung	20	18.84	1.1	92	57.26	1.6^b	60	36.61	1.6^b	40	28.96	1.4	212	141.56	1.5^b
Female breast	12	5.88	2.0^b	13	17.17	0.8	8	11.55	0.7	7	9.87	0.7	40	44.45	0.9
Female genital tract	**5**	**3.50**	**1.4**	**7**	**10.11**	**0.7**	**5**	**6.57**	**0.8**	**5**	**5.34**	**0.9**	**22**	**25.50**	**0.9**
Cervix uteri	1	0.62	1.6	0	1.72	0.0	1	1.07	0.9	0	0.83	0.0	2	4.22	0.5
Corpus uteri	2	1.42	1.4	3	4.23	0.7	2	2.77	0.7	3	2.24	1.3	10	10.65	0.9
Uterus, NOS	0	0.27	0.0	0	0.69	0.0	0	0.42	0.0	0	0.33	0.0	0	1.71	0.0
Ovary, fallopian tubes	2	0.95	2.1	4	2.78	1.4	2	1.82	1.1	2	1.50	1.3	10	7.06	1.4
Prostate gland	60	19.65	3.1^b	81	59.02	1.4^b	51	38.47	1.3	44	33.35	1.3	236	150.39	1.6^b
Testis	0	0.14	0.0	0	0.40	0.0	1	0.24	4.2	0	0.15	0.0	1	0.93	1.1
Kidney, renal pelvis, ureter	19	2.85	6.7^b	35	8.49	4.1^b	23	5.41	4.3^b	19	4.28	4.4^b	96	21.01	4.6^b
Bladder, other urinary	7	8.27	0.8	11	24.71	0.4^b	1	16.01	0.1^b	3	13.44	0.2^b	22	62.39	0.4^b
Melanoma of the skin	1	1.30	0.8	1	4.01	0.2	3	2.59	1.2	4	2.02	2.0	9	9.91	0.9
Eye	0	0.18	0.0	0	0.52	0.0	0	0.32	0.0	0	0.24	0.0	0	1.26	0.0
Brain, central nervous system	4	1.16	3.4	0	3.49	0.0	1	2.19	0.5	2	1.61	1.2	7	8.44	0.8
Thyroid gland	1	0.40	2.5	2	1.19	1.7	0	0.76	0.0	3	0.58	5.2^b	6	2.93	2.0
Bone	1	0.17	5.8	1	0.48	2.1	2	0.30	6.8	0	0.21	0.0	4	1.16	3.4
Connective tissue	0	0.59	0.0	2	1.73	1.2	4	1.11	3.6	1	0.92	1.1	7	4.35	1.6
Lymphatic, hematopoietic system	**4**	**8.25**	**0.5**	**26**	**24.71**	**1.1**	**24**	**16.04**	**1.5**	**22**	**13.44**	**1.6^b**	**76**	**62.40**	**1.2**
Non-Hodgkin's lymphoma	1	2.69	0.4	8	8.11	1.0	8	5.27	1.5	11	4.31	2.6^b	28	20.37	1.4
Hodgkin's disease	0	0.54	0.0	1	1.56	0.6	0	0.96	0.0	2	0.71	2.8	3	3.77	0.8
Multiple myeloma	0	1.31	0.0	5	3.99	1.3	4	2.61	1.5	5	2.22	2.3	14	10.13	1.4
Leukemias	3	3.70	0.8	12	11.05	1.1	12	7.19	1.7	4	6.20	0.6	31	28.12	1.1
Chronic lymphocytic	1	1.19	0.8	3	3.59	0.8	1	2.37	0.4	1	2.06	0.5	6	9.21	0.7
Acute nonlymphocytic	2	1.13	1.8	5	3.43	1.5	8	2.26	3.5^b	2	2.02	1.0	17	8.83	1.9^b

[a] ICD-O codes = 188, 189.3–189.9.

[b] $P < .05$.

BLADDER
MALES

TABLE 2D. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bladder or other urinary among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	9,139			6,997			3,341			1,452			9,139		
Person-yr in interval	6,557			19,072			11,361			7,803			44,794		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**156**	**101.97**	**1.5**[b]	**367**	**303.59**	**1.2**[b]	**231**	**192.97**	**1.2**[b]	**195**	**156.19**	**1.2**[b]	**949**	**754.21**	**1.3**[b]
All excluding site of initial cancer	**149**	**94.45**	**1.6**[b]	**358**	**281.06**	**1.3**[b]	**231**	**178.50**	**1.3**[b]	**192**	**144.18**	**1.3**[b]	**930**	**697.72**	**1.3**[b]
Buccal cavity, pharynx	**7**	**4.90**	**1.4**	**19**	**14.18**	**1.3**	**8**	**8.72**	**0.9**	**5**	**6.46**	**0.8**	**39**	**34.24**	**1.1**
Lip	1	0.90	1.1	2	2.51	0.8	0	1.52	0.0	2	1.14	1.8	5	6.06	0.8
Tongue	1	0.96	1.0	5	2.78	1.8	3	1.70	1.8	3	1.23	2.4	12	6.66	1.8
Salivary gland	0	0.26	0.0	1	0.77	1.3	0	0.48	0.0	0	0.39	0.0	1	1.91	0.5
Gum, other mouth	2	1.37	1.5	6	3.99	1.5	1	2.48	0.4	0	1.83	0.0	9	9.66	0.9
Pharynx	1	1.21	0.8	4	3.56	1.1	4	2.19	1.8	0	1.62	0.0	9	8.56	1.1
Digestive system	**30**	**32.54**	**0.9**	**94**	**95.45**	**1.0**	**59**	**60.14**	**1.0**	**41**	**48.24**	**0.8**	**224**	**236.21**	**0.9**
Esophagus	0	2.09	0.0	6	6.01	1.0	3	3.71	0.8	1	2.75	0.4	10	14.55	0.7
Stomach	5	5.87	0.9	13	16.55	0.8	11	10.13	1.1	10	7.80	1.3	39	40.32	1.0
Colon	10	12.38	0.8	35	36.98	0.9	23	23.70	1.0	15	19.73	0.8	83	92.73	0.9
Rectum	9	6.70	1.3	14	19.67	0.7	11	12.36	0.9	8	9.73	0.8	42	48.43	0.9
Liver, biliary	1	1.67	0.6	11	4.92	2.2[b]	3	3.12	1.0	1	2.56	0.4	16	12.25	1.3
Pancreas	4	3.30	1.2	13	9.76	1.3	7	6.15	1.1	6	4.90	1.2	30	24.09	1.2
Respiratory system	**24**	**20.12**	**1.2**	**94**	**60.91**	**1.5**[b]	**63**	**38.60**	**1.6**[b]	**43**	**30.16**	**1.4**[b]	**224**	**149.70**	**1.5**[b]
Nasal cavities, sinuses	2	0.21	9.3[b]	0	0.64	0.0	0	0.40	0.0	1	0.32	3.1	3	1.57	1.9
Larynx	3	2.18	1.4	8	6.44	1.2	11	3.98	2.8[b]	4	2.90	1.4	26	15.49	1.7[b]
Trachea, bronchus, lung	19	17.55	1.1	86	53.29	1.6[b]	52	33.89	1.5[b]	37	26.68	1.4	194	131.31	1.5[b]
Prostate gland	60	19.65	3.1[b]	81	59.02	1.4[b]	51	38.47	1.3	44	33.35	1.3	236	150.39	1.6[b]
Testis	0	0.14	0.0	0	0.40	0.0	1	0.24	4.2	0	0.15	0.0	1	0.93	1.1
Kidney, renal pelvis, ureter	10	2.47	4.0[b]	32	7.38	4.3[b]	13	4.65	2.8[b]	15	3.62	4.1[b]	70	18.11	3.9[b]
Bladder, other urinary	7	7.52	0.9	9	22.53	0.4[b]	0	14.47	0.0[b]	3	12.01	0.2[b]	19	56.49	0.3[b]
Melanoma of the skin	1	1.05	0.9	0	3.26	0.0	3	2.08	1.4	4	1.60	2.5	8	7.99	1.0
Eye	0	0.14	0.0	0	0.40	0.0	0	0.24	0.0	0	0.18	0.0	0	0.96	0.0
Brain, central nervous system	2	0.95	2.1	0	2.88	0.0	1	1.78	0.6	2	1.29	1.6	5	6.89	0.7
Thyroid gland	1	0.25	4.0	1	0.74	1.3	0	0.46	0.0	3	0.33	9.1[b]	5	1.78	2.8
Bone	1	0.14	7.3	1	0.39	2.6	2	0.23	8.5	0	0.16	0.0	4	0.92	4.3[b]
Connective tissue	0	0.49	0.0	1	1.45	0.7	2	0.91	2.2	1	0.75	1.3	4	3.60	1.1
Lymphatic, hematopoietic system	**4**	**6.65**	**0.6**	**24**	**19.96**	**1.2**	**18**	**12.72**	**1.4**	**17**	**10.42**	**1.6**	**63**	**49.72**	**1.3**
Non-Hodgkin's lymphoma	1	2.11	0.5	8	6.35	1.3	6	4.05	1.5	10	3.22	3.1[b]	25	15.72	1.6[b]
Hodgkin's disease	0	0.44	0.0	1	1.28	0.8	0	0.77	0.0	1	0.56	1.8	2	3.04	0.7
Multiple myeloma	0	1.03	0.0	4	3.12	1.3	2	2.01	1.0	4	1.66	2.4	10	7.81	1.3
Leukemias	3	3.08	1.0	11	9.21	1.2	10	5.89	1.7	2	4.98	0.4	26	23.14	1.1
Chronic lymphocytic	1	1.01	1.0	3	3.05	1.0	0	1.98	0.0	0	1.69	0.0	4	7.72	0.5
Acute nonlymphocytic	2	0.92	2.2	5	2.81	1.8	8	1.82	4.4[b]	1	1.60	0.6	16	7.15	2.2[b]

[a] ICD-O codes = 188, 189.3–189.9.
[b] $P < .05$.

BLADDER
FEMALES

TABLE 2E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bladder or other urinary among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,245			2,360			1,194			565			3,245		
Person-yr in interval	2,252			6,531			4,191			3,345			16,319		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**40**	**24.02**	**1.7**[b]	**60**	**69.84**	**0.9**	**60**	**47.59**	**1.3**	**42**	**41.64**	**1.0**	**202**	**182.97**	**1.1**
All excluding site of initial cancer	**40**	**23.26**	**1.7**[b]	**58**	**67.65**	**0.9**	**59**	**46.05**	**1.3**	**42**	**40.21**	**1.0**	**199**	**177.06**	**1.1**
Buccal cavity, pharynx	**0**	**0.41**	**0.0**	**0**	**1.20**	**0.0**	**0**	**0.81**	**0.0**	**0**	**0.69**	**0.0**	**0**	**3.10**	**0.0**
Lip	0	0.03	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.21	0.0
Tongue	0	0.08	0.0	0	0.24	0.0	0	0.16	0.0	0	0.14	0.0	0	0.62	0.0
Salivary gland	0	0.05	0.0	0	0.15	0.0	0	0.10	0.0	0	0.09	0.0	0	0.40	0.0
Gum, other mouth	0	0.15	0.0	0	0.43	0.0	0	0.29	0.0	0	0.25	0.0	0	1.12	0.0
Pharynx	0	0.08	0.0	0	0.25	0.0	0	0.16	0.0	0	0.13	0.0	0	0.62	0.0
Digestive system	**5**	**8.04**	**0.6**	**19**	**23.09**	**0.8**	**16**	**16.05**	**1.0**	**18**	**14.56**	**1.2**	**58**	**61.70**	**0.9**
Esophagus	0	0.17	0.0	1	0.50	2.0	0	0.35	0.0	1	0.31	3.3	2	1.33	1.5
Stomach	0	1.09	0.0	1	2.97	0.3	3	2.01	1.5	2	1.78	1.1	6	7.85	0.8
Colon	3	3.79	0.8	4	11.03	0.4[b]	6	7.74	0.8	8	7.12	1.1	21	29.67	0.7
Rectum	0	1.47	0.0	9	4.24	2.1	4	2.92	1.4	3	2.61	1.1	16	11.23	1.4
Liver, biliary	0	0.55	0.0	3	1.55	1.9	1	1.07	0.9	0	0.97	0.0	4	4.14	1.0
Pancreas	2	0.81	2.5	0	2.36	0.0	1	1.66	0.6	3	1.51	2.0	6	6.34	0.9
Respiratory system	**1**	**1.43**	**0.7**	**6**	**4.37**	**1.4**	**10**	**2.98**	**3.4**[b]	**3**	**2.49**	**1.2**	**20**	**11.26**	**1.8**[b]
Nasal cavities, sinuses	0	0.04	0.0	0	0.11	0.0	0	0.08	0.0	0	0.06	0.0	0	0.29	0.0
Larynx	0	0.08	0.0	0	0.24	0.0	2	0.16	12.8[b]	0	0.13	0.0	2	0.59	3.4
Trachea, bronchus, lung	1	1.29	0.8	6	3.97	1.5	8	2.72	2.9[b]	3	2.28	1.3	18	10.25	1.8[b]
Female breast	12	5.88	2.0[b]	13	17.17	0.8	8	11.55	0.7	7	9.87	0.7	40	44.45	0.9
Female genital tract	**5**	**3.50**	**1.4**	**7**	**10.11**	**0.7**	**5**	**6.57**	**0.8**	**5**	**5.34**	**0.9**	**22**	**25.50**	**0.9**
Cervix uteri	1	0.62	1.6	0	1.72	0.0	1	1.07	0.9	0	0.83	0.0	2	4.22	0.5
Corpus uteri	2	1.42	1.4	3	4.23	0.7	2	2.77	0.7	3	2.24	1.3	10	10.65	0.9
Uterus, NOS	0	0.27	0.0	0	0.69	0.0	0	0.42	0.0	0	0.33	0.0	0	1.71	0.0
Ovary, fallopian tubes	2	0.95	2.1	4	2.78	1.4	2	1.82	1.1	2	1.50	1.3	10	7.06	1.4
Kidney, renal pelvis, ureter	9	0.38	23.9[b]	3	1.11	2.7	10	0.76	13.2[b]	4	0.66	6.1[b]	26	2.90	9.0[b]
Bladder, other urinary	0	0.76	0.0	2	2.19	0.9	1	1.54	0.6	0	1.43	0.0	3	5.91	0.5
Melanoma of the skin	0	0.25	0.0	1	0.75	1.3	0	0.50	0.0	0	0.42	0.0	1	1.92	0.5
Eye	0	0.04	0.0	0	0.11	0.0	0	0.08	0.0	0	0.07	0.0	0	0.29	0.0
Brain, central nervous system	2	0.20	9.8[b]	0	0.62	0.0	0	0.40	0.0	0	0.32	0.0	2	1.55	1.3
Thyroid gland	0	0.15	0.0	1	0.45	2.2	0	0.30	0.0	0	0.25	0.0	1	1.16	0.9
Bone	0	0.03	0.0	0	0.09	0.0	0	0.06	0.0	0	0.05	0.0	0	0.24	0.0
Connective tissue	0	0.10	0.0	1	0.28	3.5	2	0.19	10.5[b]	0	0.17	0.0	3	0.74	4.0
Lymphatic, hematopoietic system	**0**	**1.60**	**0.0**	**2**	**4.75**	**0.4**	**6**	**3.32**	**1.8**	**5**	**3.02**	**1.7**	**13**	**12.68**	**1.0**
Non-Hodgkin's lymphoma	0	0.59	0.0	0	1.76	0.0	2	1.22	1.6	1	1.09	0.9	3	4.65	0.6
Hodgkin's disease	0	0.10	0.0	0	0.28	0.0	0	0.19	0.0	1	0.15	6.5	1	0.72	1.4
Multiple myeloma	0	0.28	0.0	1	0.86	1.2	2	0.61	3.3	1	0.56	1.8	4	2.32	1.7
Leukemias	1	0.63	0.0	1	1.84	0.5	2	1.30	1.5	2	1.22	1.6	5	4.98	1.0
Chronic lymphocytic	0	0.18	0.0	0	0.54	0.0	1	0.39	2.6	1	0.37	2.7	2	1.49	1.3
Acute nonlymphocytic	0	0.21	0.0	0	0.62	0.0	0	0.44	0.0	1	0.42	2.4	1	1.68	0.6

[a] ICD-O codes = 188, 189.3–189.9.

[b] $P < .05$.

Second Cancer Following Cutaneous Melanoma and Cancers of the Brain, Thyroid, Connective Tissue, Bone, and Eye in Connecticut, 1935–82 [1]

Margaret A. Tucker, [2] John D. Boice, Jr., [3] *and* Daniel A. Hoffman [3]

ABSTRACT—The risk of second primary cancers developing was evaluated in individuals with 6 rare tumors in Connecticut between 1935 and 1982. Small but significant excesses of all second cancers occurred in patients with cutaneous melanoma (42%), and cancers of the brain (59%), thyroid (49%), connective tissue (23%), bone (66%), and eye (40%). In individuals with cutaneous melanoma, the highest risks were for subsequent cutaneous melanomas [relative risk (RR) = 8.5] that persisted throughout all intervals of observation. The risk for second melanomas was higher in persons under age 40, consistent with a heritable component. Connective tissue tumors and breast cancers also occurred in excess. Among patients with brain cancer, an increase of melanoma was observed that may represent an underlying neural crest abnormality, although no excess of brain cancer was seen after melanoma. Reciprocal increases of bone cancer after connective tissue cancer and connective tissue cancer after bone cancer point to shared risk factors, such as high dose radiotherapy or genetic susceptibility states. An anticipated high risk of osteogenic sarcoma following Ewing's sarcoma was not seen. An excess of breast cancer (RR = 1.9) after thyroid cancer indicates common etiologic factors. Expected excesses of bilateral retinoblastoma and bone cancer after retinoblastoma were seen. Tumors commonly treated with alkylating agents or nitrosoureas (melanoma, brain, connective tissue) showed slightly elevated risks of acute nonlymphocytic leukemia. Prostate cancer was frequently found to be in excess, but this is likely an artifact due to ascertainment bias.—Natl Cancer Inst Monogr 68: 161–189, 1985.

CUTANEOUS MALIGNANT MELANOMA (ICD-O, 173, M-8720–8780)

Although cutaneous melanoma remains an uncommon tumor (2% of all incident cancers), it has become the focus of etiologic studies because of the dramatic rise in incidence over the last 50 years (*1*). Females under the age of 45 predominate as do males at older ages (*2*). Cutaneous melanoma is essentially a disease of whites; it is extremely rare in blacks, with intermediate incidence in Orientals. Overall survival has increased from 60% in 1960–63 to 79% in 1973–80 (*3*), which has been attributed largely to the earlier stage of diagnosis (*4*). The primary treatment is surgery; responses to radiation therapy or chemotherapy are poor (*5*). An earlier study of second tumors after melanoma in Connecticut revealed an excess only of cutaneous melanomas (*6*). The major etiologic factors for cutaneous melanoma are UV radiation exposure, fair complexion (*4*), family history of cutaneous melanoma (*7*), presence of dysplastic nevi (*8*), and immunosuppression (*9*). Dysplastic nevi are precursor lesions that have recently become well characterized. They occur in a familial setting, in which the trait identifies high-risk family members, and in a sporadic form, which affects about 5% of the general population. Among high-risk families, affected individuals frequently develop multiple primary melanomas (*10*). At the present time, the role of estrogens in the development of melanoma is controversial (*11–14*).

Results

Of the 4,693 persons who developed cutaneous melanoma in Connecticut between 1935 and 1982, the average age at diagnosis was 52, and the average follow-up was 5.9 years. The average year of diagnosis was 1969. Equal numbers of males and females were affected. The usual treatment for cutaneous melanoma was surgery; only 3.3% of the patients received radiation therapy. Overall, 299 persons (or 6.4%) developed second primary cancers, compared with the 211 expected, had this cohort experienced the same rates of cancer as the general population (RR = 1.41; 95% CI = 1.3–1.6).

Cutaneous melanoma accounted for 10% of all second tumors in this group (RR = 8.5; 95% CI = 5.8–12.2). The rate of second melanomas was higher in persons under age 40 at the time of original melanoma diagnosis (RR = 23; 95% CI = 13–37) than in those over age 40 (RR = 5.0; 95% CI = 2.7–8.4). The rate of second melanomas remained constant throughout all intervals, except during the first year, when the rate was highest. Significant excesses were also found for cancers of the colon, breast, kidney, thyroid, and connective tissue. Lung cancer was significantly high in females, and ANLL in males. Nonsignificant increases were observed for prostate cancer. The risk of developing a second tumor was slightly higher in females (RR = 1.5) than in males (1.3), with the excesses of colon, kidney, and lung cancers occurring primarily in women. No cancer sites occurred significantly below expectation. Among 954 patients with melanoma followed 10 or more years, excess second cancers still developed.

ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia; NOS = not otherwise specified.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Environmental Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3C29, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprints to* Margaret A. Tucker, M.D.

[3] Radiation Epidemiology Branch, Division of Cancer Etiology.

No overall differences in the risks of second cancer were observed in any of the 5-year intervals.

Discussion

Persons with cutaneous melanoma had a 42% increased risk of developing a second primary cancer throughout subsequent years of survival. The risk was highest for a second melanoma that persisted during all periods of observation. Although a small proportion of these tumors might be metastatic lesions, the majority are undoubtedly second primaries. Approximately one-third of the patients with hereditary melanoma develop multiple primary melanomas and continue to be at risk during their entire life (*10*). In these high-risk families, the only excess risk is of cutaneous melanoma (Greene MH: Unpublished observation). The higher risk of second melanoma among younger persons suggests a genetic component because heritable melanoma occurs at a younger age than do sporadic cases (*7*).

The excess of connective tissue tumors is interesting but must be viewed with caution. Differentiation of metastatic melanoma from soft tissue sarcomas, especially if it is amelanotic, can be extremely difficult. However, in a subsequent histologic review of the 7 second cancers of connective tissue in our series, 6 were classified as sarcomas and only 1 was considered a possible metastatic melanoma (Greene MH, Flannery JT, Clark WH Jr: Unpublished observations). Radiation was probably not a factor because all the connective tissue tumors occurred in patients who did not initially receive radiotherapy. It is noteworthy that melanoma was also found to be slightly increased among long-term survivors of connective tissue tumors.

The purported role of estrogens in the development of melanoma, although controversial (*11–14*), brings the observed increased risk of breast cancer to the attention of physicians. A possible association between melanoma and breast cancer is strengthened by the observation of a reciprocal excess of melanoma, including intraocular melanoma, following breast cancer in Connecticut (*15*). The increased risk of ANLL in males that occurred after 5 years may reflect exposure to chemotherapy, most commonly dacarbazine, melphalan, or the nitrosoureas, which for a time were used as adjuvant therapy for some patients with melanoma (*5*). The time to appearance is slightly longer, however, than that reported for secondary leukemias following chemotherapy for Hodgkin's disease (*16*), ovarian cancer (*17*), or gastrointestinal cancer (*18*). The slightly increased risk of prostate cancer probably reflects an artifact due to close medical surveillance and higher rates of autopsy among cancer patients than among the general population.

BRAIN (ICD-O, 191–192)

Although brain cancer accounts for only 1.5% of all incident cancers, it is the cause of 2.3% of all cancer deaths. The survival rate has remained approximately 20% at 5 years in both blacks and whites over the past 20 years (*3*). Surgery and radiation remain the primary treatment modalities with chemotherapy used increasingly (*19*). Brain cancers comprise several histologic types of tumors with separate epidemiologic characteristics. Overall, slightly more males than females develop brain cancers. Meningioma is the only common cell type occurring more frequently in women than men. Relatively little is known about the etiology of brain tumors, although genetic factors appear to be important in at least some types. Dislocations and translocations of chromosome 22 have been frequently found in meningiomas, but the meaning of these abnormalities is unknown (*19*). Individuals with neurofibromatosis, Turcot's syndrome, tuberous sclerosis, nevoid basal cell carcinoma syndrome, Cowden's disease, and other genetic disorders are at increased risk of central nervous system tumors (*20*). Relatives of children with brain cancer also have a significantly increased risk of nervous system tumors (*21*). An increased number of brain tumors were seen after radiation to the scalp for tinea capitis (*22*). Some chemicals, including vinyl chloride, have been implicated as risk factors for nervous system tumors (*20*). Excesses of brain cancers have also been reported in oil refinery workers (*23*). An earlier study in Connecticut of second tumors after brain cancer showed a significant excess of breast cancer following meningioma (*20*).

Results

Of the 3,744 individuals developing brain cancer during 1935–82 in Connecticut, 48 subsequently had a second cancer, compared with 30.3 expected (RR = 1.59; 95% CI = 1.2–2.1). The average age at diagnosis of brain cancer was 45 years, and the average year of diagnosis was 1967. The average follow-up was 2.7 years, and over 60% of the patients received radiation therapy. Approximately 60% of the cohort was male. Significant excesses of melanoma (4 observed vs. 0.7 expected) and ANLL (3 vs. 0.3) occurred as second tumors. Because of the poor survival associated with brain cancer, few second cancers occurred for any particular site.

Discussion

Although the RR is based on small numbers, the increased risk of melanoma following brain cancer may reflect an underlying abnormality in the neural crest similar to the phakomatoses (*20*) because both tumors are derived from that tissue. Whereas some brain tumors might represent a mistaken metastasis from melanoma, this does not seem likely; only 1 melanoma was diagnosed within 1 year of the brain tumor and survival with melanoma metastatic to brain is short (*5*). The increase in ANLL may be due to treatment of the brain tumor with chemotherapy, particularly the nitrosoureas (*18*). Most of the excess was seen in patients not treated with radiation, and this group might be more likely to have received chemotherapy. A heritable factor may also be involved, inasmuch as brain tumors and ANLL are associated with neurofibromatosis and with a familial syndrome of diverse types of cancer in young people (*24, 25*).

THYROID (ICD-O, 193)

Cancer of the thyroid gland is a relatively rare tumor accounting for approximately 1.2% of all new cancers diagnosed annually and about 0.2% of all cancer deaths

(*3*). However, among persons under age 45, thyroid cancer accounts for over 6% of all cancers (*2*). The incidence among females is approximately three times that in males, although this ratio varies by histologic type and age (*26*). Most thyroid cancers show either papillary or follicular cell types, which mainly affect younger people. A small proportion of patients have medullary or anaplastic types, which are more aggressive and have a higher case fatality rate. The 5-year survival rate for thyroid cancer ranges from 100% for localized papillary adenocarcinoma to 57% for regional carcinoma NOS in white females (*27*).

The only well-documented risk factor for thyroid cancer is prior exposure to ionizing radiation (*22, 28–31*). Suspected etiologic factors include diet, hormones, benign thyroid disease, and genetic susceptibility (*32*). Previous surveys of second primary cancers occurring after thyroid cancer have suggested increased risks of breast cancer (*33*) and leukemia (*34, 35*); the leukemia is linked to treatment with high doses of radioactive iodine.

Results

Of the 2,284 thyroid cancers reported between 1935 and 1982 to the Connecticut Tumor Registry, 1,681 (or 74%) occurred in females and 603 (or 26%) in males. The average age at diagnosis of thyroid cancer was 46 years. Females had a slightly longer mean follow-up period (9.1 yr) than males (7.3 yr). Most patients (79%) were treated by thyroidectomy, either with or without thyroid hormone replacement therapy. Only 21% of patients received radiation treatment. However, as the recording of subsequent treatment is incomplete, additional patients may have received radiotherapy that was not reported in the Tumor Registry records.

Overall, 169 second primary cancers were observed compared with 113 expected based on general population rates (RR = 1.49; 95% CI = 1.3–1.7). The excess risk was more pronounced in females (RR = 1.6) than in males (1.1). Second primary cancers of the breast (RR = 1.9; n = 47), kidney (RR = 4.8; n = 10), thyroid gland (RR = 4.7; n = 5), and connective tissue (RR = 5.4; n = 3) were significantly elevated over expected rates. In females, significant excesses occcurred for cancer of the pancreas (RR = 3.4; n = 7) and larynx (RR = 8.0; n = 3). The risk of a second primary cancer developing appeared to decrease with time since initial diagnosis of the thyroid cancer, and, among 797 persons followed for 10 and more years, the RR was only 1.2. However, the risk of subsequent breast cancer was elevated in every interval, though not significantly, for those followed 10 and more years. Five leukemias were reported versus 2.7 expected, and 4 of these occurred 5 or more years after thyroid cancer was diagnosed.

Discussion

Persons with thyroid cancer had a 49% excess risk of developing a second primary cancer. The excess risk was greater in females (64%) than in males (12%). The largest risk (RR = 3) of second cancers occurred within 1 year of diagnosis of thyroid cancer. This pattern could represent the effects of metastatic disease or close medical surveillance of cancer patients that would increase the likelihood of a second primary cancer diagnosis. The increased risk of breast cancer among women with thyroid cancer suggests that these cancers may share etiologic factors (*22*), particularly because thyroid cancer occurred in excess after breast cancer in Connecticut (*15*). The increased risk of kidney cancer, present in both males and females, has no obvious explanation; no excess of thyroid cancer was seen following kidney cancer in Connecticut (*36*). Radioactive iodine has been linked to small increased risks of leukemia following its use as therapy for thyroid cancer (*34, 35*) and may also have had some effect in this series.

CONNECTIVE TISSUE (ICD-O, 171)

Connective tissue cancers (or soft tissue sarcomas) account for approximately 0.6% of all cancers and for about 0.5% of all cancer deaths (*3*). The incidence is greater in blacks than whites. The incidence doubled between 1935–39 and 1965–68 in Connecticut. This same trend is shown in the mortality statistics for the United States (*37*). One of the major difficulties in epidemiologic studies of these cancers has been the failure of the ICD to categorize the variety of connective tissue cancers in a meaningful way. Many soft tissue sarcomas occur within viscera, such as uterine or bowel leiomyosarcoma, which are not included in the 171 rubric. The most common connective tissue tumors are leiomyosarcoma, liposarcoma, fibrosarcoma, and rhabdomyosarcoma. Over the years, the classification of connective tissue tumors has significantly changed, so that evaluation of time trends is difficult. The earlier study of connective tissue cancers in Connecticut demonstrated an excess risk of colon, uterus, and second connective tissue tumors (*6*).

Little is known about the etiology of connective tissue tumors, partially because of the heterogeneity of tumor types involved. A familial syndrome of multiple cancers has been described that features soft tissue sarcomas, breast cancer, and other tumors in young people (*25*). Ionizing radiation can cause connective tissue tumors but only in a small percentage of patients (*38*). Thorotrast, a radioactive contrast agent used in the early 1950s (*39*), vinyl chloride, arsenicals (*40*), and possibly androgenic steroids (*41*) can cause hepatic angiosarcomas. Herbicides which contain dioxins have also been linked to various soft tissue sarcomas (*42*). Kaposi's sarcoma, traditionally included as a connective tissue tumor, has been associated with infection by human T-cell leukemia virus type III in recent epidemics of the acquired immunodeficiency syndrome (*43*). Most connective tissue tumors are treated with surgery, radiation therapy, and chemotherapy, but the specific therapy varies with histologic type (*44*).

Results

The average age of diagnosis was 49 years for the 1,997 persons who developed connective tissue tumors during 1935–82. In this group, 152 persons developed a second primary cancer, compared with 123 expected (RR = 1.23; 95% CI = 1.04–1.44). The average follow-up was 7.7 years, and the average year of diagnosis was 1963. There was a male predominance as expected (*37*), with 56%

males and 44% females. Approximately 25% of the cohort initially received radiation therapy.

The only significantly increased risks were seen for cancers of the bone and connective tissue, with some elevation observed for colon cancer (RR = 1.5; n = 24), prostate cancer (RR = 1.6; n = 22), uterine corpus cancer (RR = 2.2; n = 7), and melanoma (RR = 2.0; n = 3). The rates of second tumors did not differ between men and women. The risk of bone cancer was higher in those treated with radiation, whereas the risk of connective tissue tumors was higher in those individuals who were not given radiotherapy.

Discussion

This survey of patients with connective tissue tumors revealed excess risks of second primary cancers of connective tissue and bone. The increase in bone cancer was doubled after radiation therapy but was also significantly high in those who were not irradiated. An increased risk of bone cancer has been reported in children after radiation treatment of soft tissue sarcomas (*45*) and among members of sarcoma-prone families who are vulnerable to spontaneous and especially radiogenic sarcomas of bone (*25*). Connective tissue tumors were also increased after bone cancer, perhaps for the same reasons, but diagnostic problems exist even if the histology of second tumors appears different. Because of the pleiomorphic appearance of many soft tissue sarcomas, exclusion of metastatic spread is often difficult, especially within the first year when the highest rate of second connective tissue cancers occurs. The increased risk of uterus and large bowel cancers could not be explained by an increase in soft tissue sarcomas of the sites, e.g., leiomyosarcomas, because none occurred. Chance events based on small numbers may be the likely explanation. The slight increases in chronic lymphocytic leukemia and prostate cancer are probably artifacts of close medical follow-up because the incidence of each was highest within the first year of follow-up. The elevated risk of ANLL may not be related to treatment because 1 of the 2 cases occurred within the first year, which would be an extremely short latency for therapy-induced leukemia. The increase in melanoma after soft tissue sarcomas is mirrored in Connecticut by an increase of soft tissue tumors following melanoma; the association between these tumors deserves further study.

BONE (ICD-O, 170)

Relatively little is known about the etiology of bone cancer, but it represents approximately 0.2% of all cancers occurring in the United States; the incidence among men and women is about the same (*3*). Radiation is the only proved environmental hazard, and certain heritable syndromes predispose to this tumor (*46*). The 5-year relative survival rate has increased slightly over the years: from 31 to 38% for men over the period 1960–63 to 1970–73 and from 31 to 36% for women over a similar period (*47*). The most common bone cancer is osteogenic sarcoma, followed by chondrosarcoma and Ewing's sarcoma. Treatment varies by type of tumor; Ewing's sarcoma is more responsive to radiotherapy and chemotherapy (*44*). An earlier survey of bone cancer in Connecticut did not find a significant risk of any second cancer (*6*).

Results

Between 1935 and 1982, a total of 839 persons developed bone cancer in Connecticut. The average age at diagnosis was 39 years, and the average follow-up was 5.2 years. The average year of diagnosis was 1961. Just a little over 41% of the patients were treated initially with radiation. Overall, 35 (or 4.2%) of all patients developed a second cancer, compared with 21.1 expected (RR = 1.66; 95% CI = 1.2–2.3). The only individual site that was significantly elevated, however, was connective tissue (2 observed vs. 0.12 expected). Other sites showing increased risks included cancers of the respiratory system and prostate, and non-Hodgkin's lymphoma and leukemia; however, all numbers were small. The overall RR were significantly elevated among men (1.9) but not for women (1.3). Risk was highest during the first year following diagnosis (RR = 2.7) and remained constant thereafter (1.5). Risk was significantly elevated among those receiving radiotherapy (RR = 2.4; 95% CI = 1.3–4.2) but not among those given other treatments (1.4; 95% CI = 0.9–2.1). Among the 144 individuals followed 10 or more years after diagnosis of bone cancer, only 14 second cancers occurred versus 9.2 expected.

Discussion

A significant 66% increased risk of developing a second cancer was observed after the diagnosis of bone cancer, with small excesses noted for cancers of the lung and prostate and for leukemia and lymphoma. Because of the rarity of bone cancer, all results for individual sites of second tumors were based on small numbers. No site was underrepresented as a second neoplasm. Radiotherapy is known to increase the incidence of soft tissue sarcoma (*38*) and may have played a role in the development of the 2 cases of connective tissue tumors in this series. It was surprising that no excess of second bone cancer was reported, contrary to reports of multicentric osteosarcomas (*46*) or of the increased risk of osteosarcomas among patients treated for Ewing's sarcoma (*45, 48*).

EYE (ICD-O, 190)

Primary cancer of the eye represents about 0.2% of all cancers occurring in the United States and 0.05% of all cancer deaths. The incidence does not vary between men and women (*3*). Eye cancer includes several different types of tumors including intraocular melanoma, retinoblastoma, orbital soft tissue sarcomas, and lacrimal gland tumors. The 5-year relative survival rate has remained fairly constant over the years, from 81 to 78% and 74 to 77% for white males and females, respectively, over the period 1960–63 to 1970–73 (*47*). Under age 15, most of the tumors are retinoblastomas; over 15, the most common tumor is intraocular melanoma. Approximately 20% of retinoblastomas are heritable and manifested by bilateral tumors. A mutation in the q14 region of chromosome 13, either constitutionally among the heritable cases or within the tumor among sporadic cases, has been linked to retinoblastoma (*49*). Children with heritable retinoblastoma are at high risk of second primary cancers, most commonly osteogenic sarcoma, either radiation-induced or spontaneous (*45, 50, 51*). Other tumors reported in excess after retinoblastoma include soft tissue sarcomas of the orbit (*45*) and cancers of the pineal (*45, 52*) and thyroid glands (*51*). Patients with retinoblastoma have a defect in DNA repair following gamma radiation that might be related to their increased propensity to develop second cancers (*53*). The primary treatment for retinoblastoma is either enucleation or external radiation therapy.

Intraocular melanoma, similar to cutaneous melanoma, is much more common among whites than blacks (*54, 55*). However, unlike cutaneous melanoma, the incidence rates have been stable over time (*56*). The major environmental risk factor for cutaneous melanoma (*4*) is UV radiation from sunlight that may affect the development of intraocular melanoma. Although most correlation analyses (*55, 57*) have not detected a significant difference in incidence rates by latitude, a recent analytic study has found a strong association between intraocular melanoma and being born and living in the southern part of the United States (*58*). This study also suggested a relation to postmenopausal estrogens. The most common treatment for intraocular melanoma is surgery, but radiation therapy is being used more frequently (*59*).

Results

From 1935 to 1982, the average age at diagnosis was 50 years for 666 individuals who developed eye cancer in Connecticut. The average year of diagnosis was 1961. An equal number of males and females was affected. In this series, 10.2% of the patients were treated with radiation. The average follow-up of 9.2 years is not unusual because of the excellent survival of patients with ocular melanoma and retinoblastoma. Overall, 68 (or 10.2%) developed second primary cancers, compared with 48.7 expected (RR = 1.40; 95% CI = 1.1–1.8). Risks were significantly elevated for cancers of the respiratory system ($n = 14$, 6.4 expected), bone (3 vs. 0.08), uterus, including NOS (6 vs. 1.6), and eye (2 vs. 0.08). Risk was significantly elevated among men (RR = 1.5) but not among women (RR = 1.2); the difference was due to the higher rate of second lung cancer in men. The higher risk of second cancers (RR = 1.9) occurred during the first year following diagnosis and decreased with time to approximately normal levels after 10 or more years of follow-up. Among the 223 individuals followed over 10 years, 19 second cancers occurred versus 17.3 expected. Only 3 second cancers were reported among the 68 persons known to have received radiotherapy, and only 1 of the 3 patients with bone cancers had received prior radiation treatment. Two of the bone cancers occurred in the skull; 1 was in the humerus.

Among 109 persons under age 15 at the time of diagnosis of eye cancer, 4 second cancers occurred, compared with 0.45 expected (RR = 8.9; 95% CI = 2.4–22.8). All the second tumors occurred in the 68 males. Two were second (contralateral) retinoblastomas that occurred 1 to 4 years after the first; the other 2 tumors were bone cancers. Another osteosarcoma occurred after radiotherapy as a third tumor in a child with bilateral retinoblastoma.

Discussion

A significant 40% excess risk of developing a second cancer was observed after the diagnosis of cancer of the eye. Although based on only 4 second tumors, children with eye cancer, primarily retinoblastoma, were at high risk of developing a second eye or bone cancer. The occurrence of bilateral retinoblastoma was not unexpected given the genetic nature of the disease (*60*). Similarly, osteosarcoma is known to be increased following retinoblastoma, especially after radiotherapy (*45, 50, 51*), and the high RR seen here might be similarly related. Radiotherapy was also given to a child with bilateral retinoblastoma who subsequently developed an osteosarcoma as a third tumor. Connective tissue and thyroid cancers were not elevated, contrary to the findings from other studies (*45, 51*); however, the number and proportion of cases receiving radiotherapy were not high in our series. Some second cancers in children treated for retinoblastoma were probably missed because of the inability of record linkage studies to match persons who moved from the geographic area of coverage and the likelihood of name changes among women who married and remained in Connecticut.

The highest risks of second tumors after adult eye cancer occurred within the first year. The increased risk of lung cancer might reflect errors in diagnosis of the eye cancer because lung cancers can metastasize to the eye and 10% of the eye tumors were not histologically confirmed. Conversely, because 22% of the second tumors were not histologically confirmed and the lung is a frequent metastatic site for intraocular melanoma, some of the excess lung cancers might represent misclassified metastatic disease. The excess of lung cancer also suggests an effect of smoking, but this is difficult for one to reconcile with the apparent lack of association between smoking and eye tumors. The elevated risk of uterine cancer after intraocular melanoma may reflect a shared hormonal factor, such as postmenopausal estrogen use. The increase in cutaneous melanoma may also reflect common risk factors, such as sunlight exposure or the dysplastic nevus syndrome.

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TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial malignant melanoma of the skin, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,336	2,357	4,693
No. who developed a second primary cancer	139	160	299
Average age at diagnosis of first cancer, yr	53	51	52
Average yr of diagnosis of first cancer	1969	1968	1969
Person-yr of follow-up	12,541	15,274	27,815
Average follow-up, yr	5.4	6.5	5.9
Percent given radiotherapy for first cancer	4.2	2.4	3.3

[a] ICD-O code = 173, morphology codes 8720–8780.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial malignant melanoma of the skin in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	275	92.0
Only the first cancer	20	6.7
Only the second cancer	3	1.0
Neither first nor second cancer	1	0.3
Total second primary cancers	299	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

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TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial malignant melanoma of the skin among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,693			3,991			1,941			954			4,693		
Person-yr in interval	3,584			11,072			6,896			6,263			27,815		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**31**	**25.52**	**1.2**	**108**	**77.71**	**1.4**^{b}	**81**	**52.27**	**1.5**^{b}	**79**	**56.01**	**1.4**^{b}	**299**	**211.38**	**1.4**^{b}
All excluding site of initial cancer	**21**	**25.10**	**0.8**	**99**	**76.39**	**1.3**^{b}	**77**	**51.39**	**1.5**^{b}	**72**	**55.12**	**1.3**^{b}	**269**	**207.87**	**1.3**^{b}
Buccal cavity, pharynx	**1**	**0.96**	**1.0**	**1**	**2.81**	**0.4**	**4**	**1.82**	**2.2**	**2**	**1.86**	**1.1**	**8**	**7.45**	**1.1**
Lip	0	0.13	0.0	0	0.33	0.0	0	0.20	0.0	1	0.18	5.5	1	0.84	1.2
Tongue	0	0.19	0.0	0	0.56	0.0	1	0.36	2.8	0	0.37	0.0	1	1.49	0.7
Salivary gland	1	0.07	15.0	0	0.20	0.0	0	0.13	0.0	0	0.13	0.0	1	0.52	1.9
Gum, other mouth	0	0.29	0.0	0	0.87	0.0	1	0.57	1.7	1	0.60	1.7	2	2.34	0.9
Pharynx	0	0.24	0.0	1	0.73	1.4	2	0.48	4.2	0	0.49	0.0	3	1.94	1.5
Digestive system	**5**	**7.38**	**0.7**	**29**	**21.94**	**1.3**	**16**	**14.65**	**1.1**	**17**	**15.89**	**1.1**	**67**	**59.82**	**1.1**
Esophagus	0	0.37	0.0	2	1.07	1.9	0	0.68	0.0	1	0.71	1.4	3	2.82	1.1
Stomach	0	1.11	0.0	2	3.11	0.6	1	1.96	0.5	2	1.99	1.0	5	8.17	0.6
Colon	3	3.07	1.0	15	9.32	1.6	10	6.35	1.6	9	7.07	1.3	37	25.79	1.4^b
Rectum	2	1.52	1.3	6	4.53	1.3	2	3.02	0.7	3	3.25	0.9	13	12.30	1.1
Liver, biliary	0	0.42	0.0	1	1.25	0.8	2	0.83	2.4	0	0.90	0.0	3	3.40	0.9
Pancreas	0	0.75	0.0	2	2.26	0.9	1	1.53	0.7	1	1.69	0.6	4	6.23	0.6
Respiratory system	**2**	**3.86**	**0.5**	**13**	**11.76**	**1.1**	**13**	**7.81**	**1.7**	**7**	**8.33**	**0.8**	**35**	**31.74**	**1.1**
Nasal cavities, sinuses	0	0.05	0.0	0	0.15	0.0	0	0.10	0.0	0	0.10	0.0	0	0.40	0.0
Larynx	0	0.40	0.0	0	1.21	0.0	2	0.78	2.6	1	0.80	1.2	3	3.19	0.9
Trachea, bronchus, lung	2	3.37	0.6	13	10.28	1.3	11	6.86	1.6	6	7.34	0.8	32	27.83	1.1
Female breast	3	3.08	1.0	16	10.37	1.5	15	7.52	2.0^b	11	8.44	1.3	45	29.39	1.5^b
Female genital tract	**3**	**1.85**	**1.6**	**4**	**6.14**	**0.7**	**7**	**4.36**	**1.6**	**7**	**4.74**	**1.5**	**21**	**17.09**	**1.2**
Cervix uteri	0	0.39	0.0	2	1.25	1.6	0	0.82	0.0	0	0.78	0.0	2	3.25	0.6
Corpus uteri	2	0.74	2.7	1	2.55	0.4	6	1.91	3.1^b	3	2.21	1.4	12	7.41	1.6
Uterus, NOS	0	0.11	0.0	1	0.32	3.2	0	0.19	0.0	1	0.17	5.8	2	0.79	2.5
Ovary, fallopian tubes	1	0.51	2.0	0	1.71	0.0	0	1.22	0.0	3	1.32	2.3	4	4.75	0.8
Prostate gland	1	2.43	0.4	13	6.62	2.0^b	3	4.10	0.7	9	4.08	2.2^b	26	17.22	1.5
Testis	0	0.06	0.0	0	0.18	0.0	0	0.10	0.0	0	0.08	0.0	0	0.43	0.0
Kidney, renal pelvis, ureter	2	0.55	3.6	3	1.68	1.8	2	1.12	1.8	3	1.18	2.5	10	4.54	2.2^b
Bladder, other urinary	1	1.35	0.7	5	3.96	1.3	2	2.61	0.8	2	2.78	0.7	10	10.69	0.9
Melanoma of the skin	10	0.42	23.6^b	9	1.32	6.8^b	4	0.88	4.6^b	7	0.89	7.9^b	30	3.51	8.5^b
Eye	0	0.04	0.0	0	0.12	0.0	0	0.08	0.0	1	0.08	12.4	1	0.32	3.1
Brain, central nervous system	1	0.32	3.1	1	1.02	1.0	1	0.68	1.5	0	0.69	0.0	3	2.71	1.1
Thyroid gland	0	0.16	0.0	1	0.53	1.9	3	0.35	8.6^b	1	0.34	3.0	5	1.38	3.6^b
Bone	0	0.04	0.0	0	0.12	0.0	0	0.07	0.0	0	0.07	0.0	0	0.30	0.0
Connective tissue	1	0.13	7.8	3	0.39	7.7^b	2	0.25	8.0	1	0.25	4.0	7	1.02	6.9^b
Lymphatic, hematopoietic system	**0**	**1.72**	**0.0**	**2**	**5.28**	**0.4**	**6**	**3.54**	**1.7**	**7**	**3.82**	**1.8**	**15**	**14.35**	**1.0**
Non-Hodgkin's lymphoma	0	0.62	0.0	1	1.93	0.5	1	1.32	0.8	1	1.45	0.7	3	5.31	0.6
Hodgkin's disease	0	0.16	0.0	0	0.49	0.0	1	0.30	3.3	1	0.28	3.6	2	1.23	1.6
Multiple myeloma	0	0.26	0.0	1	0.81	1.2	1	0.57	1.8	0	0.64	0.0	2	2.28	0.9
Leukemias	0	0.68	0.0	0	2.04	0.0	3	1.35	2.2	5	1.45	3.4^b	8	5.52	1.4
Chronic lymphocytic	0	0.20	0.0	0	0.61	0.0	0	0.41	0.0	2	0.45	4.4	2	1.68	1.2
Acute nonlymphocytic	0	0.23	0.0	0	0.69	0.0	2	0.47	4.3	3	0.52	5.8^b	5	1.91	2.6

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[a] ICD-O code = 173, morphology codes 8720–8780.

[b] $P < .05$.

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TABLE 1D. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial malignant melanoma of the skin among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,336			1,937			886			406			2,336		
Person-yr in interval	1,760			5,167			3,032			2,582			12,541		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**15**	**14.56**	**1.0**	**50**	**41.20**	**1.2**	**34**	**25.63**	**1.3**	**40**	**25.16**	**1.6**^{b}	**139**	**106.48**	**1.3**^{b}
All excluding site of initial cancer	**11**	**14.32**	**0.8**	**46**	**40.47**	**1.1**	**32**	**25.17**	**1.3**	**36**	**24.72**	**1.5**^{b}	**125**	**104.61**	**1.2**
Buccal cavity, pharynx	**1**	**0.76**	**1.3**	**1**	**2.14**	**0.5**	**2**	**1.32**	**1.5**	**2**	**1.26**	**1.6**	**6**	**5.48**	**1.1**
Lip	0	0.12	0.0	0	0.29	0.0	0	0.17	0.0	1	0.15	6.6	1	0.74	1.4
Tongue	0	0.15	0.0	0	0.43	0.0	1	0.26	3.8	0	0.25	0.0	1	1.09	0.9
Salivary gland	1	0.04	24.7	0	0.11	0.0	0	0.07	0.0	0	0.06	0.0	1	0.29	3.5
Gum, other mouth	0	0.22	0.0	0	0.64	0.0	0	0.40	0.0	1	0.39	2.6	1	1.65	0.6
Pharynx	0	0.20	0.0	1	0.58	1.7	1	0.36	2.8	0	0.35	0.0	2	1.49	1.3
Digestive system	**3**	**4.39**	**0.7**	**14**	**12.16**	**1.2**	**7**	**7.44**	**0.9**	**11**	**7.24**	**1.5**	**35**	**31.21**	**1.1**
Esophagus	0	0.29	0.0	1	0.83	1.2	0	0.50	0.0	1	0.49	2.0	2	2.11	0.9
Stomach	0	0.74	0.0	2	1.95	1.0	1	1.14	0.9	2	1.06	1.9	5	4.90	1.0
Colon	2	1.67	1.2	6	4.67	1.3	2	2.89	0.7	5	2.86	1.7	15	12.09	1.2
Rectum	1	0.93	1.1	4	2.60	1.5	2	1.60	1.2	1	1.57	0.6	8	6.70	1.2
Liver, biliary	0	0.23	0.0	1	0.63	1.6	1	0.39	2.6	0	0.37	0.0	2	1.61	1.2
Pancreas	0	0.45	0.0	0	1.26	0.0	1	0.79	1.3	1	0.76	1.3	2	3.26	0.6
Respiratory system	**1**	**3.14**	**0.3**	**7**	**9.24**	**0.8**	**8**	**5.88**	**1.4**	**1**	**5.92**	**0.2**^{b}	**17**	**24.16**	**0.7**
Nasal cavities, sinuses	0	0.03	0.0	0	0.09	0.0	0	0.05	0.0	0	0.05	0.0	0	0.23	0.0
Larynx	0	0.36	0.0	0	1.05	0.0	2	0.66	3.0	0	0.66	0.0	2	2.73	0.7
Trachea, bronchus, lung	1	2.71	0.4	7	8.01	0.9	6	5.11	1.2	1	5.15	0.2	15	20.96	0.7
Prostate gland	1	2.43	0.4	13	6.62	2.0^{b}	3	4.10	0.7	9	4.08	2.2^{b}	26	17.22	1.5
Testis	0	0.06	0.0	0	0.18	0.0	0	0.10	0.0	0	0.08	0.0	0	0.43	0.0
Kidney, renal pelvis, ureter	1	0.39	2.6	1	1.13	0.9	1	0.72	1.4	2	0.70	2.8	5	2.94	1.7
Bladder, other urinary	1	1.06	0.9	4	3.01	1.3	2	1.90	1.1	1	1.88	0.5	8	7.85	1.0
Melanoma of the skin	4	0.24	16.3^{b}	4	0.73	5.5^{b}	2	0.46	4.3	4	0.44	9.0^{b}	14	1.87	7.5^{b}
Eye	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	1	0.04	28.1	1	0.16	6.3
Brain, central nervous system	1	0.20	5.0	1	0.60	1.7	0	0.38	0.0	0	0.36	0.0	2	1.54	1.3
Thyroid gland	0	0.05	0.0	1	0.16	6.1	1	0.10	9.8	0	0.09	0.0	2	0.41	4.8
Bone	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.03	0.0	0	0.16	0.0
Connective tissue	1	0.08	12.6	2	0.23	8.7	1	0.14	7.3	1	0.13	7.8	5	0.57	8.7^{b}
Lymphatic, hematopoietic system	**0**	**1.02**	**0.0**	**1**	**2.94**	**0.3**	**5**	**1.83**	**2.7**	**5**	**1.77**	**2.8**	**11**	**7.56**	**1.5**
Non-Hodgkin's lymphoma	0	0.35	0.0	0	1.04	0.0	1	0.65	1.5	1	0.64	1.6	2	2.67	0.7
Hodgkin's disease	0	0.10	0.0	0	0.28	0.0	0	0.16	0.0	1	0.14	7.1	1	0.68	1.5
Multiple myeloma	0	0.15	0.0	1	0.42	2.4	1	0.27	3.7	0	0.27	0.0	2	1.11	1.8
Leukemias	0	0.43	0.0	0	1.20	0.0	3	0.74	4.1	3	0.72	4.2	6	3.09	1.9
Chronic lymphocytic	0	0.14	0.0	0	0.38	0.0	0	0.24	0.0	1	0.24	4.2	1	1.00	1.0
Acute nonlymphocytic	0	0.13	0.0	0	0.39	0.0	2	0.24	8.2	2	0.25	8.1	4	1.01	3.9^{b}

[a] ICD-O code = 173, morphology codes 8720–8780.

[b] $P < .05$.

MELANOMA
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial malignant melanoma of the skin among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,357			2,054			1,055			548			2,357		
Person-yr in interval	1,825			5,906			3,863			3,680			15,274		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**16**	**10.96**	**1.5**	**58**	**36.51**	**1.6**[b]	**47**	**26.64**	**1.8**[b]	**39**	**30.85**	**1.3**	**160**	**104.89**	**1.5**[b]
All excluding site of initial cancer	**10**	**10.78**	**0.9**	**53**	**35.92**	**1.5**[b]	**45**	**26.22**	**1.7**[b]	**36**	**30.40**	**1.2**	**144**	**103.25**	**1.4**[b]
Buccal cavity, pharynx	**0**	**0.20**	**0.0**	**0**	**0.68**	**0.0**	**2**	**0.50**	**4.0**	**0**	**0.60**	**0.0**	**2**	**1.97**	**1.0**
Lip	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.03	0.0	0	0.10	0.0
Tongue	0	0.04	0.0	0	0.14	0.0	0	0.10	0.0	0	0.12	0.0	0	0.40	0.0
Salivary gland	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.07	0.0	0	0.24	0.0
Gum, other mouth	0	0.07	0.0	0	0.23	0.0	1	0.17	5.8	0	0.21	0.0	1	0.69	1.5
Pharynx	0	0.05	0.0	0	0.15	0.0	1	0.12	8.6	0	0.14	0.0	1	0.45	2.2
Digestive system	**2**	**2.99**	**0.7**	**15**	**9.78**	**1.5**	**9**	**7.21**	**1.2**	**6**	**8.65**	**0.7**	**32**	**28.61**	**1.1**
Esophagus	0	0.07	0.0	1	0.24	4.2	0	0.18	0.0	0	0.22	0.0	1	0.71	1.4
Stomach	0	0.37	0.0	0	1.16	0.0	0	0.82	0.0	0	0.93	0.0	0	3.27	0.0
Colon	1	1.41	0.7	9	4.64	1.9	8	3.46	2.3	4	4.20	1.0	22	13.70	1.6[b]
Rectum	1	0.59	1.7	2	1.93	1.0	0	1.41	0.0	2	1.68	1.2	5	5.60	0.9
Liver, biliary	0	0.19	0.0	0	0.62	0.0	1	0.45	2.2	0	0.53	0.0	1	1.79	0.6
Pancreas	0	0.30	0.0	2	0.99	2.0	0	0.75	0.0	0	0.93	0.0	2	2.97	0.7
Respiratory system	**1**	**0.73**	**1.4**	**6**	**2.52**	**2.4**	**5**	**1.93**	**2.6**	**6**	**2.41**	**2.5**	**18**	**7.59**	**2.4**[b]
Nasal cavities, sinuses	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.17	0.0
Larynx	0	0.04	0.0	0	0.15	0.0	0	0.12	0.0	1	0.14	7.0	1	0.46	2.2
Trachea, bronchus, lung	1	0.65	1.5	6	2.28	2.6	5	1.75	2.9	5	2.20	2.3	17	6.87	2.5[b]
Female breast	3	3.08	1.0	16	10.37	1.5	15	7.52	2.0[b]	11	8.44	1.3	45	29.39	1.5[b]
Female genital tract	**3**	**1.85**	**1.6**	**4**	**6.14**	**0.7**	**7**	**4.36**	**1.6**	**7**	**4.74**	**1.5**	**21**	**17.09**	**1.2**
Cervix uteri	0	0.39	0.0	2	1.25	1.6	0	0.82	0.0	0	0.78	0.0	2	3.25	0.6
Corpus uteri	2	0.74	2.7	1	2.55	0.4	6	1.91	3.1[b]	3	2.21	1.4	12	7.41	1.6
Uterus, NOS	0	0.11	0.0	1	0.32	3.2	0	0.19	0.0	1	0.17	5.8	2	0.79	2.5
Ovary, fallopian tubes	1	0.51	2.0	0	1.71	0.0	0	1.22	0.0	3	1.32	2.3	4	4.75	0.8
Kidney, renal pelvis, ureter	1	0.16	6.1	2	0.55	3.6	1	0.41	2.5	1	0.48	2.1	5	1.60	3.1[b]
Bladder, other urinary	0	0.29	0.0	1	0.95	1.1	0	0.72	0.0	1	0.90	1.1	2	2.84	0.7
Melanoma of the skin	6	0.18	33.5[b]	5	0.59	8.4[b]	2	0.42	4.8	3	0.45	6.7[b]	16	1.64	9.8[b]
Eye	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.16	0.0
Brain, central nervous system	0	0.12	0.0	0	0.42	0.0	1	0.30	3.4	0	0.33	0.0	1	1.17	0.9
Thyroid gland	0	0.11	0.0	0	0.37	0.0	2	0.25	8.1	1	0.24	4.1	3	0.97	3.1
Bone	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.14	0.0
Connective tissue	0	0.05	0.0	1	0.16	6.2	1	0.11	8.8	0	0.12	0.0	2	0.45	4.5
Lymphatic, hematopoietic system	**0**	**0.70**	**0.0**	**1**	**2.34**	**0.4**	**1**	**1.72**	**0.6**	**2**	**2.04**	**1.0**	**4**	**6.79**	**0.6**
Non-Hodgkin's lymphoma	0	0.27	0.0	1	0.90	1.1	0	0.67	0.0	0	0.81	0.0	1	2.64	0.4
Hodgkin's disease	0	0.07	0.0	0	0.21	0.0	1	0.14	7.1	0	0.13	0.0	1	0.55	1.8
Multiple myeloma	0	0.11	0.0	0	0.39	0.0	0	0.30	0.0	0	0.37	0.0	0	1.17	0.0
Leukemias	0	0.25	0.0	0	0.84	0.0	0	0.61	0.0	2	0.73	2.7	2	2.43	0.8
Chronic lymphocytic	0	0.07	0.0	0	0.23	0.0	0	0.17	0.0	1	0.21	4.7	1	0.68	1.5
Acute nonlymphocytic	0	0.09	0.0	0	0.30	0.0	0	0.23	0.0	1	0.27	3.7	1	0.89	1.1

[a] ICD-O code = 173, morphology codes 8720–8780.

[b] $P < .05$.

EYE
BOTH SEXES

TABLE 2A. *Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the eye, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	346	320	666
No. who developed a second primary cancer	41	27	68
Average age at diagnosis of first cancer, yr	49	51	50
Average yr of diagnosis of first cancer	1961	1961	1961
Person-yr of follow-up	2,897	3,223	6,120
Average follow-up, yr	8.4	10.1	9.2
Percent given radiotherapy for first cancer	11.3	9.1	10.2

[a] ICD-O code = 190.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the eye in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	49	72.1
Only the first cancer	12	17.6
Only the second cancer	4	5.9
Neither first nor second cancer	3	4.4
Total second primary cancers	68	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

EYE
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the eye among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	666			611			386			223			666		
Person-yr in interval	532			1,936			1,460			2,191			6,120		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8**	**4.23**	**1.9**	**27**	**15.47**	**1.7**[b]	**14**	**11.73**	**1.2**	**19**	**17.29**	**1.1**	**68**	**48.69**	**1.4**[b]
All excluding site of initial cancer	**8**	**4.22**	**1.9**	**25**	**15.44**	**1.6**[b]	**14**	**11.71**	**1.2**	**19**	**17.27**	**1.1**	**66**	**48.61**	**1.4**[b]
Buccal cavity, pharynx	**0**	**0.17**	**0.0**	**0**	**0.59**	**0.0**	**0**	**0.43**	**0.0**	**1**	**0.55**	**1.8**	**1**	**1.74**	**0.6**
Lip	0	0.03	0.0	0	0.10	0.0	0	0.07	0.0	0	0.09	0.0	0	0.29	0.0
Tongue	0	0.03	0.0	0	0.12	0.0	0	0.09	0.0	1	0.11	9.0	1	0.35	2.9
Salivary gland	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0
Gum, other mouth	0	0.05	0.0	0	0.17	0.0	0	0.12	0.0	0	0.16	0.0	0	0.50	0.0
Pharynx	0	0.04	0.0	0	0.14	0.0	0	0.10	0.0	0	0.13	0.0	0	0.41	0.0
Digestive system	**1**	**1.38**	**0.7**	**8**	**4.94**	**1.6**	**3**	**3.75**	**0.8**	**5**	**5.54**	**0.9**	**17**	**15.58**	**1.1**
Esophagus	0	0.07	0.0	0	0.24	0.0	0	0.18	0.0	0	0.23	0.0	0	0.73	0.0
Stomach	0	0.25	0.0	1	0.85	1.2	1	0.62	1.6	0	0.86	0.0	2	2.57	0.8
Colon	0	0.54	0.0	0	1.98	0.0	1	1.55	0.6	2	2.38	0.8	3	6.44	0.5
Rectum	1	0.28	3.6	4	0.99	4.0[b]	0	0.74	0.0	1	1.07	0.9	6	3.08	2.0
Liver, biliary	0	0.08	0.0	1	0.29	3.5	0	0.22	0.0	1	0.33	3.0	2	0.92	2.2
Pancreas	0	0.14	0.0	2	0.49	4.1	1	0.37	2.7	0	0.56	0.0	3	1.56	1.9
Respiratory system	**2**	**0.57**	**3.5**	**3**	**2.13**	**1.4**	**7**	**1.61**	**4.3**[b]	**2**	**2.13**	**0.9**	**14**	**6.44**	**2.2**[b]
Nasal cavities, sinuses	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Larynx	0	0.06	0.0	0	0.23	0.0	0	0.17	0.0	0	0.20	0.0	0	0.66	0.0
Trachea, bronchus, lung	2	0.49	4.1	3	1.85	1.6	7	1.41	5.0[b]	2	1.87	1.1	14	5.62	2.5[b]
Female breast	1	0.45	2.2	3	1.67	1.8	0	1.22	0.0	1	2.03	0.5	5	5.37	0.9
Female genital tract	**1**	**0.30**	**3.3**	**3**	**1.10**	**2.7**	**1**	**0.79**	**1.3**	**2**	**1.22**	**1.6**	**7**	**3.40**	**2.1**
Cervix uteri	0	0.07	0.0	0	0.23	0.0	0	0.16	0.0	1	0.23	4.3	1	0.69	1.4
Corpus uteri	0	0.11	0.0	1	0.42	2.4	1	0.31	3.2	1	0.48	2.1	3	1.33	2.3
Uterus, NOS	1	0.03	37.7	2	0.09	23.0[b]	0	0.06	0.0	0	0.08	0.0	3	0.25	11.9[b]
Ovary, fallopian tubes	0	0.08	0.0	0	0.29	0.0	0	0.21	0.0	0	0.34	0.0	0	0.92	0.0
Prostate gland	0	0.43	0.0	0	1.57	0.0	0	1.28	0.0	2	1.84	1.1	2	5.12	0.4
Testis	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.03	0.0	0	0.07	0.0
Kidney, renal pelvis, ureter	0	0.09	0.0	0	0.33	0.0	0	0.24	0.0	0	0.34	0.0	0	1.00	0.0
Bladder, other urinary	2	0.22	9.1[b]	1	0.81	1.2	0	0.63	0.0	1	0.93	1.1	4	2.58	1.5
Melanoma of the skin	0	0.04	0.0	1	0.17	5.9	1	0.12	8.1	0	0.20	0.0	2	0.53	3.7
Eye	0	0.01	0.0	2	0.03	67.7[b]	0	0.02	0.0	0	0.02	0.0	2	0.08	24.1[b]
Brain, central nervous system	0	0.05	0.0	0	0.17	0.0	0	0.12	0.0	0	0.16	0.0	0	0.50	0.0
Thyroid gland	0	0.02	0.0	1	0.07	13.9	0	0.05	0.0	0	0.10	0.0	1	0.24	4.1
Bone	0	0.01	0.0	1	0.03	36.7	1	0.02	51.9	1	0.03	33.6	3	0.08	35.7[b]
Connective tissue	0	0.02	0.0	0	0.08	0.0	0	0.06	0.0	0	0.09	0.0	0	0.24	0.0
Lymphatic, hematopoietic system	**1**	**0.27**	**3.7**	**1**	**1.01**	**1.0**	**1**	**0.79**	**1.3**	**1**	**1.22**	**0.8**	**4**	**3.29**	**1.2**
Non-Hodgkin's lymphoma	1	0.09	11.1	0	0.34	0.0	0	0.26	0.0	0	0.40	0.0	1	1.09	0.9
Hodgkin's disease	0	0.02	0.0	0	0.08	0.0	0	0.06	0.0	0	0.11	0.0	0	0.27	0.0
Multiple myeloma	0	0.04	0.0	0	0.16	0.0	0	0.12	0.0	0	0.19	0.0	0	0.51	0.0
Leukemias	0	0.12	0.0	1	0.43	2.3	1	0.35	2.9	1	0.52	1.9	3	1.42	2.1
Chronic lymphocytic	0	0.03	0.0	0	0.12	0.0	0	0.10	0.0	0	0.16	0.0	0	0.42	0.0
Acute nonlymphocytic	0	0.03	0.0	1	0.13	7.7	0	0.11	0.0	1	0.16	6.1	2	0.44	4.6

[a] ICD-O code = 190.

[b] $P < .05$.

BRAIN
BOTH SEXES

TABLE 3A. *Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the brain or central nervous system, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,171	1,573	3,744
No. who developed a second primary cancer	26	22	48
Average age at diagnosis of first cancer, yr	45	45	45
Average yr of diagnosis of first cancer	1967	1968	1967
Person-yr of follow-up	5,455	4,552	10,008
Average follow-up, yr	2.5	2.9	2.7
Percent given radiotherapy for first cancer	64.1	60.9	62.8

[a] ICD-O codes = 191–192.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the brain or central nervous system in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	39	81.3
Only the first cancer	4	8.3
Only the second cancer	3	6.3
Neither first nor second cancer	2	4.2
Total second primary cancers	48	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

BRAIN
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the brain or central nervous system among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,744			1,648			565			307			3,744		
Person-yr in interval	1,997			3,463			2,065			2,483			10,008		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**16**	**9.05**	**1.8**[b]	**13**	**9.00**	**1.4**	**7**	**5.20**	**1.3**	**12**	**7.02**	**1.7**	**48**	**30.25**	**1.6**[b]
All excluding site of initial cancer	**16**	**8.89**	**1.8**[b]	**13**	**8.81**	**1.5**	**6**	**5.10**	**1.2**	**11**	**6.89**	**1.6**	**46**	**29.66**	**1.6**[b]
Buccal cavity, pharynx	**0**	**0.39**	**0.0**	**0**	**0.37**	**0.0**	**0**	**0.19**	**0.0**	**1**	**0.27**	**3.8**	**1**	**1.21**	**0.8**
Lip	0	0.05	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.14	0.0
Tongue	0	0.08	0.0	0	0.08	0.0	0	0.04	0.0	0	0.05	0.0	0	0.25	0.0
Salivary gland	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	1	0.02	47.1	1	0.09	11.4
Gum, other mouth	0	0.12	0.0	0	0.11	0.0	0	0.06	0.0	0	0.08	0.0	0	0.37	0.0
Pharynx	0	0.11	0.0	0	0.10	0.0	0	0.05	0.0	0	0.07	0.0	0	0.33	0.0
Digestive system	**2**	**2.42**	**0.8**	**3**	**2.21**	**1.4**	**1**	**1.28**	**0.8**	**0**	**1.73**	**0.0**	**6**	**7.64**	**0.8**
Esophagus	0	0.14	0.0	0	0.13	0.0	0	0.07	0.0	0	0.09	0.0	0	0.42	0.0
Stomach	1	0.34	2.9	1	0.31	3.2	0	0.17	0.0	0	0.23	0.0	2	1.06	1.9
Colon	0	0.97	0.0	2	0.89	2.2	1	0.53	1.9	0	0.72	0.0	3	3.12	1.0
Rectum	0	0.53	0.0	0	0.48	0.0	0	0.27	0.0	0	0.37	0.0	0	1.66	0.0
Liver, biliary	0	0.13	0.0	0	0.12	0.0	0	0.07	0.0	0	0.09	0.0	0	0.41	0.0
Pancreas	0	0.26	0.0	0	0.23	0.0	0	0.13	0.0	0	0.18	0.0	0	0.80	0.0
Respiratory system	**2**	**1.60**	**1.2**	**1**	**1.40**	**0.7**	**1**	**0.73**	**1.4**	**2**	**1.07**	**1.9**	**6**	**4.80**	**1.2**
Nasal cavities, sinuses	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Larynx	0	0.18	0.0	0	0.16	0.0	0	0.08	0.0	1	0.12	8.6	1	0.54	1.9
Trachea, bronchus, lung	2	1.39	1.4	1	1.21	0.8	1	0.64	1.6	1	0.92	1.1	5	4.15	1.2
Female breast	0	1.05	0.0	3	1.34	2.2	1	0.87	1.2	1	1.01	1.0	5	4.27	1.2
Female genital tract	**2**	**0.67**	**3.0**	**1**	**0.86**	**1.2**	**0**	**0.54**	**0.0**	**2**	**0.63**	**3.2**	**5**	**2.69**	**1.9**
Cervix uteri	0	0.14	0.0	0	0.21	0.0	0	0.13	0.0	0	0.14	0.0	0	0.62	0.0
Corpus uteri	1	0.28	3.5	0	0.34	0.0	0	0.22	0.0	1	0.26	3.8	2	1.10	1.8
Uterus, NOS	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Ovary, fallopian tubes	1	0.18	5.4	1	0.24	4.2	0	0.15	0.0	0	0.18	0.0	2	0.75	2.7
Prostate gland	3	0.68	4.4	1	0.49	2.0	0	0.26	0.0	1	0.44	2.3	5	1.87	2.7
Testis	0	0.04	0.0	0	0.06	0.0	0	0.03	0.0	0	0.07	0.0	0	0.20	0.0
Kidney, renal pelvis, ureter	0	0.22	0.0	0	0.21	0.0	0	0.11	0.0	0	0.15	0.0	0	0.70	0.0
Bladder, other urinary	0	0.46	0.0	0	0.39	0.0	0	0.22	0.0	0	0.32	0.0	0	1.39	0.0
Melanoma of the skin	1	0.17	6.0	1	0.20	5.0	2	0.11	18.0[b]	0	0.17	0.0	4	0.65	6.1[b]
Eye	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Brain, central nervous system	0	0.16	0.0	0	0.19	0.0	1	0.10	9.6	1	0.13	7.6	2	0.59	3.4
Thyroid gland	0	0.06	0.0	1	0.09	10.9	0	0.06	0.0	1	0.08	11.8	2	0.29	6.8
Bone	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Connective tissue	0	0.05	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.20	0.0
Lymphatic, hematopoietic system	**3**	**0.65**	**4.6**	**2**	**0.71**	**2.8**	**1**	**0.42**	**2.4**	**1**	**0.58**	**1.7**	**7**	**2.35**	**3.0**[b]
Non-Hodgkin's lymphoma	0	0.24	0.0	0	0.25	0.0	0	0.14	0.0	0	0.20	0.0	0	0.83	0.0
Hodgkin's disease	1	0.08	13.2	0	0.11	0.0	0	0.07	0.0	0	0.12	0.0	1	0.38	2.6
Multiple myeloma	1	0.09	11.0	0	0.08	0.0	0	0.05	0.0	1	0.07	14.4	2	0.29	6.8
Leukemias	1	0.24	4.1	2	0.26	7.7	1	0.15	6.7	0	0.20	0.0	4	0.85	4.7[b]
Chronic lymphocytic	0	0.07	0.0	0	0.06	0.0	0	0.03	0.0	0	0.05	0.0	0	0.20	0.0
Acute nonlymphocytic	0	0.08	0.0	2	0.09	22.7[b]	1	0.05	18.7	0	0.07	0.0	3	0.30	10.1[b]

[a] ICD-O codes = 191–192.

[b] $P < .05$.

BRAIN
MALES

TABLE 3D. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the brain or central nervous system among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,171			927			305			165			2,171		
Person-yr in interval	1,154			1,884			1,080			1,338			5,455		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**11**	**5.46**	**2.0**[b]	**4**	**4.65**	**0.9**	**5**	**2.33**	**2.1**	**6**	**3.58**	**1.7**	**26**	**16.02**	**1.6**[b]
All excluding site of initial cancer	**11**	**5.35**	**2.1**[b]	**4**	**4.53**	**0.9**	**4**	**2.27**	**1.8**	**6**	**3.50**	**1.7**	**25**	**15.66**	**1.6**[b]
Buccal cavity, pharynx	**0**	**0.32**	**0.0**	**0**	**0.29**	**0.0**	**0**	**0.14**	**0.0**	**0**	**0.20**	**0.0**	**0**	**0.94**	**0.0**
Lip	0	0.04	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.12	0.0
Tongue	0	0.06	0.0	0	0.06	0.0	0	0.03	0.0	0	0.04	0.0	0	0.19	0.0
Salivary gland	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Gum, other mouth	0	0.09	0.0	0	0.08	0.0	0	0.04	0.0	0	0.06	0.0	0	0.28	0.0
Pharynx	0	0.09	0.0	0	0.08	0.0	0	0.04	0.0	0	0.05	0.0	0	0.26	0.0
Digestive system	**2**	**1.57**	**1.3**	**1**	**1.30**	**0.8**	**0**	**0.64**	**0.0**	**0**	**0.96**	**0.0**	**3**	**4.46**	**0.7**
Esophagus	0	0.12	0.0	0	0.10	0.0	0	0.05	0.0	0	0.07	0.0	0	0.34	0.0
Stomach	1	0.25	4.0	0	0.22	0.0	0	0.11	0.0	0	0.15	0.0	1	0.72	1.4
Colon	0	0.57	0.0	1	0.46	2.2	0	0.23	0.0	0	0.36	0.0	1	1.62	0.6
Rectum	0	0.35	0.0	0	0.29	0.0	0	0.14	0.0	0	0.21	0.0	0	0.99	0.0
Liver, biliary	0	0.08	0.0	0	0.07	0.0	0	0.03	0.0	0	0.05	0.0	0	0.23	0.0
Pancreas	0	0.17	0.0	0	0.14	0.0	0	0.07	0.0	0	0.10	0.0	0	0.48	0.0
Respiratory system	**2**	**1.33**	**1.5**	**1**	**1.10**	**0.9**	**1**	**0.54**	**1.9**	**1**	**0.82**	**1.2**	**5**	**3.79**	**1.3**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.16	0.0	0	0.14	0.0	0	0.07	0.0	0	0.10	0.0	0	0.47	0.0
Trachea, bronchus, lung	2	1.14	1.8	1	0.94	1.1	1	0.46	2.2	1	0.70	1.4	5	3.24	1.5
Prostate gland	3	0.68	4.4	1	0.49	2.0	0	0.26	0.0	1	0.44	2.3	5	1.87	2.7
Testis	0	0.04	0.0	0	0.06	0.0	0	0.03	0.0	0	0.07	0.0	0	0.20	0.0
Kidney, renal pelvis, ureter	0	0.17	0.0	0	0.15	0.0	0	0.07	0.0	0	0.10	0.0	0	0.49	0.0
Bladder, other urinary	0	0.38	0.0	0	0.31	0.0	0	0.15	0.0	0	0.24	0.0	0	1.08	0.0
Melanoma of the skin	0	0.11	0.0	0	0.11	0.0	2	0.05	36.6[b]	0	0.09	0.0	2	0.37	5.4
Eye	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Brain, central nervous system	0	0.11	0.0	0	0.12	0.0	1	0.06	16.9	0	0.08	0.0	1	0.36	2.7
Thyroid gland	0	0.03	0.0	1	0.03	33.7	0	0.02	0.0	1	0.03	37.7	2	0.10	20.5[b]
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.04	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.12	0.0
Lymphatic, hematopoietic system	**2**	**0.42**	**4.7**	**0**	**0.42**	**0.0**	**1**	**0.22**	**4.5**	**1**	**0.34**	**3.0**	**4**	**1.40**	**2.8**
Non-Hodgkin's lymphoma	0	0.15	0.0	0	0.15	0.0	0	0.07	0.0	0	0.11	0.0	0	0.48	0.0
Hodgkin's disease	0	0.05	0.0	0	0.07	0.0	0	0.05	0.0	0	0.07	0.0	0	0.24	0.0
Multiple myeloma	1	0.06	18.0	0	0.05	0.0	0	0.02	0.0	1	0.04	27.7	2	0.16	12.5[b]
Leukemias	1	0.16	6.1	0	0.16	0.0	1	0.08	12.0	0	0.12	0.0	2	0.53	3.8
Chronic lymphocytic	0	0.05	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.13	0.0
Acute nonlymphocytic	0	0.05	0.0	0	0.05	0.0	1	0.03	36.0	0	0.04	0.0	1	0.17	5.8

[a] ICD-O codes = 191–192.

[b] $P < .05$.

BRAIN
FEMALES

TABLE 3E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the brain or central nervous system among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,573			721			260			142			1,573		
Person-yr in interval	843			1,580			985			1,145			4,552		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**5**	**3.59**	**1.4**	**9**	**4.34**	**2.1**	**2**	**2.87**	**0.7**	**6**	**3.44**	**1.7**	**22**	**14.23**	**1.5**
All excluding site of initial cancer	**5**	**3.54**	**1.4**	**9**	**4.27**	**2.1**	**2**	**2.83**	**0.7**	**5**	**3.39**	**1.5**	**21**	**14.01**	**1.5**
Buccal cavity, pharynx	**0**	**0.07**	**0.0**	**0**	**0.08**	**0.0**	**0**	**0.05**	**0.0**	**1**	**0.07**	**15.2**	**1**	**0.27**	**3.7**
Lip	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Tongue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Salivary gland	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	1	0.01	107.0[b]	1	0.04	27.1
Gum, other mouth	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Pharynx	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.07	0.0
Digestive system	**0**	**0.85**	**0.0**	**2**	**0.91**	**2.2**	**1**	**0.64**	**1.6**	**0**	**0.77**	**0.0**	**3**	**3.18**	**0.9**
Esophagus	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Stomach	0	0.09	0.0	1	0.10	10.1	0	0.07	0.0	0	0.08	0.0	1	0.34	3.0
Colon	0	0.40	0.0	1	0.43	2.3	1	0.31	3.3	0	0.36	0.0	2	1.50	1.3
Rectum	0	0.18	0.0	0	0.19	0.0	0	0.13	0.0	0	0.16	0.0	0	0.67	0.0
Liver, biliary	0	0.05	0.0	0	0.05	0.0	0	0.04	0.0	0	0.05	0.0	0	0.19	0.0
Pancreas	0	0.09	0.0	0	0.09	0.0	0	0.07	0.0	0	0.08	0.0	0	0.32	0.0
Respiratory system	**0**	**0.27**	**0.0**	**0**	**0.30**	**0.0**	**0**	**0.19**	**0.0**	**1**	**0.25**	**4.1**	**1**	**1.01**	**1.0**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0
Larynx	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	1	0.02	61.7	1	0.07	15.1
Trachea, bronchus, lung	0	0.24	0.0	0	0.27	0.0	0	0.17	0.0	0	0.22	0.0	0	0.91	0.0
Female breast	0	1.05	0.0	3	1.34	2.2	1	0.87	1.2	1	1.01	1.0	5	4.27	1.2
Female genital tract	**2**	**0.67**	**3.0**	**1**	**0.86**	**1.2**	**0**	**0.54**	**0.0**	**2**	**0.63**	**3.2**	**5**	**2.69**	**1.9**
Cervix uteri	0	0.14	0.0	0	0.21	0.0	0	0.13	0.0	0	0.14	0.0	0	0.62	0.0
Corpus uteri	1	0.28	3.5	0	0.34	0.0	0	0.22	0.0	1	0.26	3.8	2	1.10	1.8
Uterus, NOS	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Ovary, fallopian tubes	1	0.18	5.4	1	0.24	4.2	0	0.15	0.0	0	0.18	0.0	2	0.75	2.7
Kidney, renal pelvis, ureter	0	0.06	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.21	0.0
Bladder, other urinary	0	0.08	0.0	0	0.09	0.0	0	0.06	0.0	0	0.08	0.0	0	0.31	0.0
Melanoma of the skin	1	0.06	16.7	1	0.09	11.4	0	0.06	0.0	0	0.08	0.0	2	0.28	7.1
Eye	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0
Brain, central nervous system	0	0.05	0.0	0	0.07	0.0	0	0.04	0.0	1	0.05	19.3	1	0.22	4.5
Thyroid gland	0	0.04	0.0	0	0.06	0.0	0	0.04	0.0	0	0.06	0.0	0	0.20	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Connective tissue	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Lymphatic, hematopoietic system	**1**	**0.23**	**4.4**	**2**	**0.29**	**7.0**	**0**	**0.19**	**0.0**	**0**	**0.24**	**0.0**	**3**	**0.95**	**3.2**
Non-Hodgkin's lymphoma	0	0.09	0.0	0	0.10	0.0	0	0.07	0.0	0	0.09	0.0	0	0.35	0.0
Hodgkin's disease	1	0.03	39.9	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	1	0.14	7.0
Multiple myeloma	0	0.04	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Leukemias	0	0.08	0.0	2	0.10	20.2[b]	0	0.07	0.0	0	0.08	0.0	2	0.32	6.2
Chronic lymphocytic	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.07	0.0
Acute nonlymphocytic	0	0.03	0.0	2	0.04	53.2[b]	0	0.03	0.0	0	0.03	0.0	2	0.13	16.0[b]

[a] ICD-O codes = 191–192.

[b] $P < .05$.

THYROID
BOTH SEXES

TABLE 4A. *Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the thyroid gland, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	603	1,681	2,284
No. who developed a second primary cancer	35	134	169
Average age at diagnosis of first cancer, yr	48	46	46
Average yr of diagnosis of first cancer	1968	1967	1967
Person-yr of follow-up	4,380	15,320	19,700
Average follow-up, yr	7.3	9.1	8.6
Percent given radiotherapy for first cancer	24.7	19.8	21.1

[a] ICD-O code = 193.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B. *Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the thyroid gland in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	150	88.8
Only the first cancer	14	8.3
Only the second cancer	3	1.8
Neither first nor second cancer	2	1.2
Total second primary cancers	169	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

THYROID
BOTH SEXES

TABLE 4C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the thyroid gland among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,284			1,960			1,312			797			2,284		
Person-yr in interval	1,729			6,406			5,125			6,439			19,700		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**24**	**8.05**	**3.0**[b]	**49**	**29.63**	**1.7**[b]	**37**	**27.84**	**1.3**	**59**	**47.66**	**1.2**	**169**	**113.12**	**1.5**[b]
All excluding site of initial cancer	**22**	**7.96**	**2.8**[b]	**47**	**29.30**	**1.6**[b]	**36**	**27.56**	**1.3**	**59**	**47.28**	**1.2**	**164**	**112.06**	**1.5**[b]
Buccal cavity, pharynx	**0**	**0.25**	**0.0**	**3**	**0.91**	**3.3**	**0**	**0.81**	**0.0**	**0**	**1.28**	**0.0**	**3**	**3.24**	**0.9**
Lip	0	0.03	0.0	1	0.10	9.8	0	0.08	0.0	0	0.10	0.0	1	0.31	3.2
Tongue	0	0.05	0.0	0	0.18	0.0	0	0.16	0.0	0	0.26	0.0	0	0.65	0.0
Salivary gland	0	0.02	0.0	0	0.08	0.0	0	0.07	0.0	0	0.11	0.0	0	0.28	0.0
Gum, other mouth	0	0.08	0.0	1	0.28	3.6	0	0.25	0.0	0	0.42	0.0	1	1.03	1.0
Pharynx	0	0.06	0.0	1	0.23	4.4	0	0.21	0.0	0	0.33	0.0	1	0.83	1.2
Digestive system	**3**	**2.20**	**1.4**	**14**	**7.68**	**1.8**	**5**	**7.08**	**0.7**	**17**	**12.27**	**1.4**	**39**	**29.21**	**1.3**
Esophagus	0	0.09	0.0	0	0.33	0.0	0	0.29	0.0	2	0.46	4.4	2	1.16	1.7
Stomach	0	0.33	0.0	2	1.08	1.8	1	0.91	1.1	0	1.36	0.0	3	3.68	0.8
Colon	1	0.93	1.1	6	3.30	1.8	2	3.14	0.6	10	5.67	1.8	19	13.03	1.5
Rectum	0	0.44	0.0	4	1.59	2.5	0	1.47	0.0	3	2.55	1.2	7	6.05	1.2
Liver, biliary	0	0.13	0.0	0	0.45	0.0	0	0.41	0.0	1	0.69	1.4	1	1.68	0.6
Pancreas	2	0.22	9.2[b]	2	0.77	2.6	2	0.72	2.8	1	1.31	0.8	7	3.02	2.3
Respiratory system	**3**	**0.88**	**3.4**	**1**	**3.39**	**0.3**	**2**	**3.23**	**0.6**	**6**	**5.57**	**1.1**	**12**	**13.07**	**0.9**
Nasal cavities, sinuses	0	0.02	0.0	0	0.06	0.0	0	0.05	0.0	0	0.08	0.0	0	0.20	0.0
Larynx	1	0.09	11.0	0	0.34	0.0	0	0.31	0.0	3	0.47	6.3[b]	4	1.21	3.3
Trachea, bronchus, lung	2	0.76	2.6	1	2.96	0.3	2	2.84	0.7	3	4.96	0.6	8	11.52	0.7
Female breast	5	1.60	3.1[b]	15	6.05	2.5[b]	13	5.89	2.2[b]	14	10.75	1.3	47	24.27	1.9[b]
Female genital tract	**0**	**1.00**	**0.0**	**5**	**3.74**	**1.3**	**3**	**3.52**	**0.9**	**2**	**6.21**	**0.3**	**10**	**14.46**	**0.7**
Cervix uteri	0	0.25	0.0	0	0.92	0.0	0	0.80	0.0	0	1.11	0.0	0	3.08	0.0
Corpus uteri	0	0.37	0.0	2	1.43	1.4	2	1.43	1.4	0	2.89	0.0	4	6.11	0.7
Uterus, NOS	0	0.06	0.0	0	0.20	0.0	0	0.15	0.0	0	0.19	0.0	0	0.60	0.0
Ovary, fallopian tubes	0	0.27	0.0	3	1.03	2.9	0	0.98	0.0	2	1.74	1.2	5	4.02	1.2
Prostate gland	2	0.36	5.6	0	1.37	0.0	0	1.34	0.0	3	1.74	1.7	5	4.81	1.0
Testis	0	0.02	0.0	0	0.07	0.0	0	0.05	0.0	0	0.04	0.0	0	0.17	0.0
Kidney, renal pelvis, ureter	3	0.15	19.9[b]	1	0.55	1.8	3	0.52	5.8[b]	3	0.88	3.4	10	2.10	4.8[b]
Bladder, other urinary	0	0.30	0.0	2	1.12	1.8	2	1.06	1.9	2	1.76	1.1	6	4.24	1.4
Melanoma of the skin	1	0.14	7.0	1	0.56	1.8	0	0.52	0.0	1	0.80	1.3	3	2.02	1.5
Eye	0	0.01	0.0	0	0.05	0.0	0	0.04	0.0	0	0.07	0.0	0	0.18	0.0
Brain, central nervous system	0	0.11	0.0	0	0.41	0.0	1	0.38	2.7	2	0.61	3.3	3	1.51	2.0
Thyroid gland	2	0.09	22.7[b]	2	0.33	6.2	1	0.28	3.6	0	0.38	0.0	5	1.06	4.7[b]
Bone	1	0.02	66.3	0	0.05	0.0	0	0.04	0.0	0	0.06	0.0	1	0.16	6.1
Connective tissue	2	0.04	45.5[b]	1	0.16	6.2	0	0.14	0.0	0	0.20	0.0	3	0.55	5.4[b]
Lymphatic, hematopoietic system	**2**	**0.54**	**3.7**	**1**	**1.97**	**0.5**	**3**	**1.82**	**1.6**	**6**	**3.10**	**1.9**	**12**	**7.43**	**1.6**
Non-Hodgkin's lymphoma	1	0.19	5.2	0	0.72	0.0	1	0.69	1.5	2	1.22	1.6	4	2.81	1.4
Hodgkin's disease	1	0.07	14.2	0	0.25	0.0	0	0.20	0.0	0	0.25	0.0	1	0.77	1.3
Multiple myeloma	0	0.07	0.0	0	0.28	0.0	1	0.28	3.6	1	0.54	1.9	2	1.16	1.7
Leukemias	0	0.20	0.0	1	0.72	1.4	1	0.66	1.5	3	1.10	2.7	5	2.68	1.9
Chronic lymphocytic	0	0.05	0.0	0	0.19	0.0	0	0.18	0.0	1	0.33	3.1	1	0.75	1.3
Acute nonlymphocytic	0	0.07	0.0	0	0.25	0.0	1	0.24	4.2	2	0.41	4.9	3	0.96	3.1

[a] ICD-O code = 193.
[b] $P < .05$.

THYROID
MALES

TABLE 4D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the thyroid gland among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	603			506			312			168			603		
Person-yr in interval	449			1,604			1,154			1,173			4,380		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8**	**2.53**	**3.2**[b]	**7**	**9.47**	**0.7**	**6**	**8.44**	**0.7**	**14**	**10.95**	**1.3**	**35**	**31.37**	**1.1**
All excluding site of initial cancer	**8**	**2.52**	**3.2**[b]	**6**	**9.42**	**0.6**	**6**	**8.40**	**0.7**	**14**	**10.91**	**1.3**	**34**	**31.23**	**1.1**
Buccal cavity, pharynx	**0**	**0.15**	**0.0**	**1**	**0.54**	**1.9**	**0**	**0.44**	**0.0**	**0**	**0.55**	**0.0**	**1**	**1.68**	**0.6**
Lip	0	0.02	0.0	0	0.08	0.0	0	0.06	0.0	0	0.07	0.0	0	0.24	0.0
Tongue	0	0.03	0.0	0	0.11	0.0	0	0.09	0.0	0	0.11	0.0	0	0.33	0.0
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Gum, other mouth	0	0.04	0.0	1	0.16	6.4	0	0.13	0.0	0	0.17	0.0	1	0.50	2.0
Pharynx	0	0.04	0.0	0	0.14	0.0	0	0.12	0.0	0	0.16	0.0	0	0.46	0.0
Digestive system	**1**	**0.77**	**1.3**	**2**	**2.84**	**0.7**	**0**	**2.47**	**0.0**	**4**	**3.14**	**1.3**	**7**	**9.22**	**0.8**
Esophagus	0	0.06	0.0	0	0.21	0.0	0	0.17	0.0	1	0.21	4.7	1	0.65	1.5
Stomach	0	0.14	0.0	1	0.50	2.0	0	0.39	0.0	0	0.45	0.0	1	1.49	0.7
Colon	1	0.27	3.7	1	1.03	1.0	0	0.94	0.0	2	1.24	1.6	4	3.47	1.2
Rectum	0	0.17	0.0	0	0.61	0.0	0	0.53	0.0	1	0.68	1.5	1	2.00	0.5
Liver, biliary	0	0.04	0.0	0	0.15	0.0	0	0.13	0.0	0	0.16	0.0	0	0.48	0.0
Pancreas	0	0.08	0.0	0	0.30	0.0	0	0.26	0.0	0	0.33	0.0	0	0.98	0.0
Respiratory system	**1**	**0.55**	**1.8**	**0**	**2.10**	**0.0**	**2**	**1.90**	**1.0**	**1**	**2.61**	**0.4**	**4**	**7.16**	**0.6**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Larynx	0	0.07	0.0	0	0.26	0.0	0	0.22	0.0	1	0.29	3.4	1	0.83	1.2
Trachea, bronchus, lung	1	0.47	2.1	0	1.80	0.0	2	1.65	1.2	0	2.27	0.0	3	6.19	0.5
Prostate gland	2	0.36	5.6	0	1.37	0.0	0	1.34	0.0	3	1.74	1.7	5	4.81	1.0
Testis	0	0.02	0.0	0	0.07	0.0	0	0.05	0.0	0	0.04	0.0	0	0.17	0.0
Kidney, renal pelvis, ureter	1	0.07	14.0	0	0.26	0.0	1	0.23	4.3	1	0.31	3.2	3	0.88	3.4
Bladder, other urinary	0	0.17	0.0	1	0.66	1.5	0	0.61	0.0	2	0.81	2.5	3	2.26	1.3
Melanoma of the skin	0	0.05	0.0	1	0.17	5.8	0	0.15	0.0	1	0.19	5.2	2	0.56	3.6
Eye	0	0.00	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Brain, central nervous system	0	0.04	0.0	0	0.15	0.0	1	0.13	7.9	0	0.16	0.0	1	0.48	2.1
Thyroid gland	0	0.01	0.0	1	0.05	21.8	0	0.04	0.0	0	0.04	0.0	1	0.14	7.3
Bone	1	0.01	191.7[b]	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	1	0.05	19.2
Connective tissue	2	0.02	126.1[b]	1	0.06	17.0	0	0.05	0.0	0	0.06	0.0	3	0.18	16.7[b]
Lymphatic, hematopoietic system	**0**	**0.19**	**0.0**	**0**	**0.70**	**0.0**	**1**	**0.61**	**1.6**	**1**	**0.77**	**1.3**	**2**	**2.28**	**0.9**
Non-Hodgkin's lymphoma	0	0.06	0.0	0	0.24	0.0	0	0.21	0.0	0	0.28	0.0	0	0.79	0.0
Hodgkin's disease	0	0.02	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.24	0.0
Multiple myeloma	0	0.02	0.0	0	0.09	0.0	1	0.09	11.5	0	0.12	0.0	1	0.33	3.1
Leukemias	0	0.08	0.0	0	0.28	0.0	0	0.25	0.0	1	0.31	3.2	1	0.92	1.1
Chronic lymphocytic	0	0.02	0.0	0	0.09	0.0	0	0.08	0.0	0	0.10	0.0	0	0.29	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.09	0.0	0	0.08	0.0	1	0.11	9.3	1	0.29	3.4

[a] ICD-O code = 193.

[b] $P < .05$.

THYROID
FEMALES

TABLE 4E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the thyroid gland among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,681			1,454			1,000			629			1,681		
Person-yr in interval	1,281			4,801			3,971			5,267			15,320		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**16**	**5.52**	**2.9**[b]	**42**	**20.16**	**2.1**[b]	**31**	**19.40**	**1.6**[b]	**45**	**36.70**	**1.2**	**134**	**81.75**	**1.6**[b]
All excluding site of initial cancer	**14**	**5.45**	**2.6**[b]	**41**	**19.88**	**2.1**[b]	**30**	**19.16**	**1.6**[b]	**45**	**36.37**	**1.2**	**130**	**80.82**	**1.6**[b]
Buccal cavity, pharynx	**0**	**0.10**	**0.0**	**2**	**0.37**	**5.4**	**0**	**0.36**	**0.0**	**0**	**0.73**	**0.0**	**2**	**1.56**	**1.3**
Lip	0	0.00	0.0	1	0.02	58.0	0	0.02	0.0	0	0.03	0.0	1	0.07	14.2
Tongue	0	0.02	0.0	0	0.07	0.0	0	0.07	0.0	0	0.15	0.0	0	0.32	0.0
Salivary gland	0	0.01	0.0	0	0.05	0.0	0	0.05	0.0	0	0.08	0.0	0	0.20	0.0
Gum, other mouth	0	0.03	0.0	0	0.12	0.0	0	0.12	0.0	0	0.25	0.0	0	0.53	0.0
Pharynx	0	0.02	0.0	1	0.09	11.6	0	0.09	0.0	0	0.18	0.0	1	0.37	2.7
Digestive system	**2**	**1.42**	**1.4**	**12**	**4.83**	**2.5**[b]	**5**	**4.61**	**1.1**	**13**	**9.13**	**1.4**	**32**	**19.99**	**1.6**[b]
Esophagus	0	0.03	0.0	0	0.12	0.0	0	0.12	0.0	1	0.25	4.1	1	0.52	1.9
Stomach	0	0.19	0.0	1	0.59	1.7	1	0.52	1.9	0	0.90	0.0	2	2.19	0.9
Colon	0	0.66	0.0	5	2.27	2.2	2	2.20	0.9	8	4.43	1.8	15	9.56	1.6
Rectum	0	0.28	0.0	4	0.97	4.1[b]	0	0.94	0.0	2	1.87	1.1	6	4.05	1.5
Liver, biliary	0	0.09	0.0	0	0.31	0.0	0	0.28	0.0	1	0.53	1.9	1	1.21	0.8
Pancreas	2	0.14	14.6[b]	2	0.47	4.2	2	0.46	4.4	1	0.98	1.0	7	2.05	3.4[b]
Respiratory system	**2**	**0.33**	**6.0**	**1**	**1.29**	**0.8**	**0**	**1.33**	**0.0**	**5**	**2.96**	**1.7**	**8**	**5.91**	**1.4**
Nasal cavities, sinuses	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.06	0.0	0	0.14	0.0
Larynx	1	0.02	46.9	0	0.08	0.0	0	0.09	0.0	2	0.18	10.9[b]	3	0.38	8.0[b]
Trachea, bronchus, lung	1	0.30	3.4	1	1.15	0.9	0	1.19	0.0	3	2.69	1.1	5	5.33	0.9
Female breast	5	1.60	3.1[b]	15	6.05	2.5[b]	13	5.89	2.2[b]	14	10.75	1.3	47	24.27	1.9[b]
Female genital tract	**0**	**1.00**	**0.0**	**5**	**3.74**	**1.3**	**3**	**3.52**	**0.9**	**2**	**6.21**	**0.3**	**10**	**14.46**	**0.7**
Cervix uteri	0	0.25	0.0	0	0.92	0.0	0	0.80	0.0	0	1.11	0.0	0	3.08	0.0
Corpus uteri	0	0.37	0.0	2	1.43	1.4	2	1.43	1.4	0	2.89	0.0	4	6.11	0.7
Uterus, NOS	0	0.06	0.0	0	0.20	0.0	0	0.15	0.0	0	0.19	0.0	0	0.60	0.0
Ovary, fallopian tubes	0	0.27	0.0	3	1.03	2.9	0	0.98	0.0	2	1.74	1.2	5	4.02	1.2
Kidney, renal pelvis, ureter	2	0.08	25.2[b]	1	0.29	3.5	2	0.28	7.1	2	0.57	3.5	7	1.22	5.7[b]
Bladder, other urinary	0	0.13	0.0	1	0.45	2.2	2	0.45	4.4	0	0.95	0.0	3	1.98	1.5
Melanoma of the skin	1	0.10	10.3	0	0.39	0.0	0	0.37	0.0	0	0.61	0.0	1	1.47	0.7
Eye	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.06	0.0	0	0.13	0.0
Brain, central nervous system	0	0.07	0.0	0	0.26	0.0	0	0.25	0.0	2	0.45	4.5	2	1.03	1.9
Thyroid gland	2	0.07	26.8[b]	1	0.28	3.6	1	0.24	4.2	0	0.33	0.0	4	0.93	4.3[b]
Bone	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.04	0.0	0	0.11	0.0
Connective tissue	0	0.03	0.0	0	0.10	0.0	0	0.09	0.0	0	0.15	0.0	0	0.37	0.0
Lymphatic, hematopoietic system	**2**	**0.35**	**5.7**	**1**	**1.27**	**0.8**	**2**	**1.21**	**1.7**	**5**	**2.33**	**2.1**	**10**	**5.16**	**1.9**
Non-Hodgkin's lymphoma	1	0.13	7.8	0	0.48	0.0	1	0.47	2.1	2	0.94	2.1	4	2.02	2.0
Hodgkin's disease	1	0.05	21.6	0	0.17	0.0	0	0.14	0.0	0	0.18	0.0	1	0.54	1.9
Multiple myeloma	0	0.05	0.0	0	0.18	0.0	0	0.19	0.0	1	0.42	2.4	1	0.84	1.2
Leukemias	0	0.12	0.0	1	0.44	2.3	1	0.41	2.4	2	0.78	2.6	4	1.76	2.3
Chronic lymphocytic	0	0.03	0.0	0	0.10	0.0	0	0.10	0.0	1	0.22	4.5	1	0.46	2.2
Acute nonlymphocytic	0	0.05	0.0	0	0.16	0.0	1	0.16	6.3	1	0.30	3.3	2	0.67	3.0

[a] ICD-O code = 193.

[b] $P < .05$.

BONE
BOTH SEXES

TABLE 5A. *Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the bone, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	465	374	839
No. who developed a second primary cancer	24	11	35
Average age at diagnosis of first cancer, yr	39	39	39
Average yr of diagnosis of first cancer	1961	1961	1961
Person-yr of follow-up	2,296	2,106	4,402
Average follow-up, yr	4.9	5.6	5.2
Percent given radiotherapy for first cancer	39.8	44.1	41.7

[a] ICD-O code = 170.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 5B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the bone in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	24	68.6
Only the first cancer	4	11.4
Only the second cancer	5	14.3
Neither first nor second cancer	2	5.7
Total second primary cancers	35	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

BONE
BOTH SEXES

TABLE 5C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bone among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	839			553			236			144			839		
Person-yr in interval	557			1,398			923			1,525			4,402		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**6**	**2.25**	**2.7**	**8**	**5.47**	**1.5**	**7**	**4.20**	**1.7**	**14**	**9.20**	**1.5**	**35**	**21.11**	**1.7**[b]
All excluding site of initial cancer	**5**	**2.24**	**2.2**	**8**	**5.45**	**1.5**	**7**	**4.19**	**1.7**	**14**	**9.19**	**1.5**	**34**	**21.06**	**1.6**[b]
Buccal cavity, pharynx	**0**	**0.09**	**0.0**	**0**	**0.23**	**0.0**	**0**	**0.17**	**0.0**	**0**	**0.34**	**0.0**	**0**	**0.83**	**0.0**
Lip	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.13	0.0
Tongue	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.07	0.0	0	0.17	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Gum, other mouth	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.10	0.0	0	0.24	0.0
Pharynx	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.09	0.0	0	0.21	0.0
Digestive system	**1**	**0.70**	**1.4**	**2**	**1.62**	**1.2**	**0**	**1.23**	**0.0**	**3**	**2.56**	**1.2**	**6**	**6.11**	**1.0**
Esophagus	0	0.04	0.0	0	0.09	0.0	0	0.07	0.0	0	0.13	0.0	0	0.33	0.0
Stomach	0	0.13	0.0	1	0.29	3.5	0	0.20	0.0	1	0.37	2.7	2	0.99	2.0
Colon	1	0.27	3.8	1	0.62	1.6	0	0.49	0.0	0	1.08	0.0	2	2.46	0.8
Rectum	0	0.14	0.0	0	0.34	0.0	0	0.25	0.0	1	0.53	1.9	1	1.27	0.8
Liver, biliary	0	0.04	0.0	0	0.09	0.0	0	0.07	0.0	0	0.14	0.0	0	0.34	0.0
Pancreas	0	0.07	0.0	0	0.16	0.0	0	0.12	0.0	0	0.26	0.0	0	0.61	0.0
Respiratory system	**1**	**0.31**	**3.2**	**1**	**0.79**	**1.3**	**1**	**0.62**	**1.6**	**4**	**1.40**	**2.9**	**7**	**3.12**	**2.2**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Larynx	1	0.04	27.7	0	0.09	0.0	0	0.07	0.0	1	0.14	7.0	2	0.34	5.8
Trachea, bronchus, lung	0	0.27	0.0	1	0.68	1.5	1	0.53	1.9	3	1.22	2.5	5	2.70	1.9
Female breast	0	0.23	0.0	0	0.55	0.0	1	0.48	2.1	1	1.12	0.9	2	2.38	0.8
Female genital tract	**0**	**0.16**	**0.0**	**0**	**0.38**	**0.0**	**1**	**0.31**	**3.3**	**2**	**0.70**	**2.9**	**3**	**1.55**	**1.9**
Cervix uteri	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	1	0.15	6.5	1	0.37	2.7
Corpus uteri	0	0.06	0.0	0	0.14	0.0	1	0.11	9.1	0	0.29	0.0	1	0.59	1.7
Uterus, NOS	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	1	0.03	32.0	1	0.09	11.0
Ovary, fallopian tubes	0	0.04	0.0	0	0.10	0.0	0	0.09	0.0	0	0.19	0.0	0	0.42	0.0
Prostate gland	1	0.22	4.5	1	0.55	1.8	1	0.39	2.5	1	0.90	1.1	4	2.06	1.9
Testis	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Kidney, renal pelvis, ureter	1	0.05	21.3	0	0.12	0.0	0	0.09	0.0	0	0.20	0.0	1	0.46	2.2
Bladder, other urinary	0	0.11	0.0	0	0.28	0.0	0	0.22	0.0	1	0.48	2.1	1	1.10	0.9
Melanoma of the skin	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.16	0.0	0	0.33	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Brain, central nervous system	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	1	0.12	8.1	1	0.29	3.4
Thyroid gland	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.07	0.0	0	0.15	0.0
Bone	1	0.01	119.2[b]	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	1	0.05	20.1
Connective tissue	0	0.01	0.0	0	0.03	0.0	2	0.03	79.5[b]	0	0.05	0.0	2	0.12	16.4[b]
Lymphatic, hematopoietic system	**1**	**0.16**	**6.3**	**3**	**0.39**	**7.7**[b]	**0**	**0.30**	**0.0**	**1**	**0.64**	**1.6**	**5**	**1.49**	**3.4**[b]
Non-Hodgkin's lymphoma	1	0.05	19.1	1	0.13	7.7	0	0.10	0.0	0	0.23	0.0	2	0.51	4.0
Hodgkin's disease	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.07	0.0	0	0.19	0.0
Multiple myeloma	0	0.02	0.0	1	0.05	20.5	0	0.04	0.0	0	0.10	0.0	1	0.21	4.9
Leukemias	0	0.06	0.0	1	0.16	6.4	0	0.12	0.0	1	0.25	4.0	2	0.59	3.4
Chronic lymphocytic	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.07	0.0	0	0.16	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	1	0.08	11.9	1	0.19	5.3

[a] ICD-O code = 170.

[b] $P < .05$.

BONE
MALES

TABLE 5D. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bone among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	465			308			125			73			465		
Person-yr in interval	309			765			469			752			2,296		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**1.38**	**2.9**	**7**	**3.48**	**2.0**	**4**	**2.51**	**1.6**	**9**	**5.35**	**1.7**	**24**	**12.72**	**1.9**[b]
All excluding site of initial cancer	**3**	**1.37**	**2.2**	**7**	**3.47**	**2.0**	**4**	**2.50**	**1.6**	**9**	**5.34**	**1.7**	**23**	**12.69**	**1.8**[b]
Buccal cavity, pharynx	**0**	**0.08**	**0.0**	**0**	**0.20**	**0.0**	**0**	**0.14**	**0.0**	**0**	**0.27**	**0.0**	**0**	**0.69**	**0.0**
Lip	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.04	0.0	0	0.12	0.0
Tongue	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.14	0.0
Salivary gland	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Gum, other mouth	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.08	0.0	0	0.19	0.0
Pharynx	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.07	0.0	0	0.17	0.0
Digestive system	**0**	**0.45**	**0.0**	**2**	**1.12**	**1.8**	**0**	**0.78**	**0.0**	**3**	**1.60**	**1.9**	**5**	**3.95**	**1.3**
Esophagus	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.10	0.0	0	0.28	0.0
Stomach	0	0.10	0.0	1	0.22	4.4	0	0.15	0.0	1	0.26	3.8	2	0.73	2.7
Colon	0	0.15	0.0	1	0.39	2.6	0	0.28	0.0	0	0.62	0.0	1	1.44	0.7
Rectum	0	0.10	0.0	0	0.24	0.0	0	0.17	0.0	1	0.34	3.0	1	0.84	1.2
Liver, biliary	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.08	0.0	0	0.20	0.0
Pancreas	0	0.04	0.0	0	0.11	0.0	0	0.08	0.0	0	0.17	0.0	0	0.40	0.0
Respiratory system	**0**	**0.26**	**0.0**	**1**	**0.68**	**1.5**	**1**	**0.52**	**1.9**	**3**	**1.14**	**2.6**	**5**	**2.60**	**1.9**
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Larynx	0	0.03	0.0	0	0.09	0.0	0	0.06	0.0	1	0.13	7.9	1	0.31	3.2
Trachea, bronchus, lung	0	0.22	0.0	1	0.57	1.7	1	0.45	2.2	2	0.99	2.0	4	2.23	1.8
Prostate gland	1	0.22	4.5	1	0.55	1.8	1	0.39	2.5	1	0.90	1.1	4	2.06	1.9
Testis	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Kidney, renal pelvis, ureter	1	0.03	29.3	0	0.09	0.0	0	0.07	0.0	0	0.14	0.0	1	0.33	3.0
Bladder, other urinary	0	0.09	0.0	0	0.24	0.0	0	0.18	0.0	1	0.39	2.6	1	0.90	1.1
Melanoma of the skin	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.09	0.0	0	0.19	0.0
Eye	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0
Brain, central nervous system	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	1	0.07	13.6	1	0.18	5.5
Thyroid gland	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Bone	1	0.01	188.4[b]	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	1	0.03	32.3
Connective tissue	0	0.01	0.0	0	0.02	0.0	1	0.02	63.8	0	0.03	0.0	1	0.08	12.8
Lymphatic, hematopoietic system	**1**	**0.10**	**9.9**	**3**	**0.26**	**11.5**[b]	**0**	**0.18**	**0.0**	**0**	**0.39**	**0.0**	**4**	**0.94**	**4.3**[b]
Non-Hodgkin's lymphoma	1	0.03	31.1	1	0.08	12.0	0	0.06	0.0	0	0.13	0.0	2	0.30	6.6
Hodgkin's disease	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0
Multiple myeloma	0	0.01	0.0	1	0.03	32.0	0	0.02	0.0	0	0.06	0.0	1	0.12	8.1
Leukemias	0	0.04	0.0	1	0.11	9.1	0	0.08	0.0	0	0.16	0.0	1	0.39	2.5
Chronic lymphocytic	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.05	0.0	0	0.11	0.0
Acute nonlymphocytic	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.05	0.0	0	0.12	0.0

[a] ICD-O code = 170.

[b] $P < .05$.

BONE
FEMALES

TABLE 5E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bone among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	374			245			111			71			374		
Person-yr in interval	247			633			454			773			2,106		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**0.87**	**2.3**	**1**	**1.98**	**0.5**	**3**	**1.69**	**1.8**	**5**	**3.85**	**1.3**	**11**	**8.39**	**1.3**
All excluding site of initial cancer	**2**	**0.87**	**2.3**	**1**	**1.97**	**0.5**	**3**	**1.69**	**1.8**	**5**	**3.84**	**1.3**	**11**	**8.37**	**1.3**
Buccal cavity, pharynx	**0**	**0.01**	**0.0**	**0**	**0.03**	**0.0**	**0**	**0.03**	**0.0**	**0**	**0.07**	**0.0**	**0**	**0.15**	**0.0**
Lip	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Tongue	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Salivary gland	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0
Gum, other mouth	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Pharynx	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.03	0.0
Digestive system	**1**	**0.25**	**4.1**	**0**	**0.51**	**0.0**	**0**	**0.45**	**0.0**	**0**	**0.96**	**0.0**	**1**	**2.16**	**0.5**
Esophagus	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Stomach	0	0.03	0.0	0	0.06	0.0	0	0.06	0.0	0	0.11	0.0	0	0.26	0.0
Colon	1	0.11	9.0	0	0.23	0.0	0	0.21	0.0	0	0.46	0.0	1	1.02	1.0
Rectum	0	0.05	0.0	0	0.10	0.0	0	0.09	0.0	0	0.19	0.0	0	0.43	0.0
Liver, biliary	0	0.02	0.0	0	0.03	0.0	0	0.03	0.0	0	0.06	0.0	0	0.14	0.0
Pancreas	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.10	0.0	0	0.21	0.0
Respiratory system	**1**	**0.05**	**20.3**	**0**	**0.12**	**0.0**	**0**	**0.09**	**0.0**	**1**	**0.26**	**3.9**	**2**	**0.52**	**3.9**
Nasal cavities, sinuses	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0
Larynx	1	0.00	336.9[b]	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	1	0.03	30.1
Trachea, bronchus, lung	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	1	0.23	4.3	1	0.46	2.2
Female breast	0	0.23	0.0	0	0.55	0.0	1	0.48	2.1	1	1.12	0.9	2	2.38	0.8
Female genital tract	**0**	**0.16**	**0.0**	**0**	**0.38**	**0.0**	**1**	**0.31**	**3.3**	**2**	**0.70**	**2.9**	**3**	**1.55**	**1.9**
Cervix uteri	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	1	0.15	6.5	1	0.37	2.7
Corpus uteri	0	0.06	0.0	0	0.14	0.0	1	0.11	9.1	0	0.29	0.0	1	0.59	1.7
Uterus, NOS	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	1	0.03	32.0	1	0.09	11.0
Ovary, fallopian tubes	0	0.04	0.0	0	0.10	0.0	0	0.09	0.0	0	0.19	0.0	0	0.42	0.0
Kidney, renal pelvis, ureter	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.06	0.0	0	0.12	0.0
Bladder, other urinary	0	0.02	0.0	0	0.04	0.0	0	0.04	0.0	0	0.09	0.0	0	0.20	0.0
Melanoma of the skin	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.07	0.0	0	0.14	0.0
Eye	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0
Brain, central nervous system	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.05	0.0	0	0.11	0.0
Thyroid gland	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.10	0.0
Bone	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0
Connective tissue	0	0.00	0.0	0	0.01	0.0	1	0.01	105.6[b]	0	0.02	0.0	1	0.04	22.8
Lymphatic, hematopoietic system	**0**	**0.06**	**0.0**	**0**	**0.13**	**0.0**	**0**	**0.11**	**0.0**	**1**	**0.25**	**4.0**	**1**	**0.55**	**1.8**
Non-Hodgkin's lymphoma	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.09	0.0	0	0.20	0.0
Hodgkin's disease	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.07	0.0
Multiple myeloma	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.08	0.0
Leukemias	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	1	0.08	11.9	1	0.19	5.2
Chronic lymphocytic	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Acute nonlymphocytic	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	1	0.03	32.2	1	0.07	14.5

[a] ICD-O code = 170.

[b] $P < .05$.

CONNECTIVE TISSUE
BOTH SEXES

TABLE 6A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial cancer of the connective tissue, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,112	885	1,997
No. who developed a second primary cancer	92	60	152
Average age at diagnosis of first cancer, yr	50	49	49
Average yr of diagnosis of first cancer	1963	1962	1963
Person-yr of follow-up	8,011	7,371	15,382
Average follow-up, yr	7.2	8.3	7.7
Percent given radiotherapy for first cancer	25.7	23.8	24.9

[a] ICD-O code = 171.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 6B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the connective tissue in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	124	81.6
Only the first cancer	21	13.8
Only the second cancer	5	3.3
Neither first nor second cancer	2	1.3
Total second primary cancers	152	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

CONNECTIVE TISSUE
BOTH SEXES

TABLE 6C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the connective tissue among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval Person-yr in interval	1,997 1,446			1,583 4,652			902 3,667			597 5,617			1,997 15,382		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**18**	**10.75**	**1.7**	**43**	**34.37**	**1.3**	**27**	**28.57**	**0.9**	**64**	**49.72**	**1.3**	**152**	**123.35**	**1.2**[b]
All excluding site of initial cancer	**17**	**10.69**	**1.6**	**42**	**34.19**	**1.2**	**27**	**28.43**	**0.9**	**62**	**49.48**	**1.3**	**148**	**122.72**	**1.2**[b]
Buccal cavity, pharynx	**0**	**0.42**	**0.0**	**0**	**1.36**	**0.0**	**1**	**1.12**	**0.9**	**2**	**1.73**	**1.2**	**3**	**4.64**	**0.6**
Lip	0	0.08	0.0	0	0.24	0.0	1	0.19	5.2	1	0.25	4.0	2	0.76	2.6
Tongue	0	0.08	0.0	0	0.27	0.0	0	0.22	0.0	1	0.34	2.9	1	0.92	1.1
Salivary gland	0	0.03	0.0	0	0.09	0.0	0	0.08	0.0	0	0.12	0.0	0	0.32	0.0
Gum, other mouth	0	0.12	0.0	0	0.39	0.0	0	0.32	0.0	0	0.52	0.0	0	1.35	0.0
Pharynx	0	0.10	0.0	0	0.32	0.0	0	0.27	0.0	0	0.43	0.0	0	1.12	0.0
Digestive system	**3**	**3.44**	**0.9**	**16**	**10.85**	**1.5**	**9**	**8.82**	**1.0**	**17**	**14.98**	**1.1**	**45**	**38.08**	**1.2**
Esophagus	0	0.18	0.0	0	0.56	0.0	0	0.45	0.0	0	0.70	0.0	0	1.89	0.0
Stomach	1	0.62	1.6	2	1.93	1.0	3	1.50	2.0	3	2.18	1.4	9	6.22	1.4
Colon	1	1.36	0.7	9	4.30	2.1	6	3.57	1.7	8	6.43	1.2	24	15.65	1.5
Rectum	1	0.69	1.5	1	2.18	0.5	0	1.77	0.0	3	3.00	1.0	5	7.63	0.7
Liver, biliary	0	0.20	0.0	0	0.61	0.0	0	0.49	0.0	0	0.85	0.0	0	2.15	0.0
Pancreas	0	0.34	0.0	2	1.07	1.9	0	0.88	0.0	3	1.56	1.9	5	3.85	1.3
Respiratory system	**2**	**1.51**	**1.3**	**6**	**4.90**	**1.2**	**5**	**4.10**	**1.2**	**8**	**6.99**	**1.1**	**21**	**17.50**	**1.2**
Nasal cavities, sinuses	0	0.02	0.0	0	0.07	0.0	0	0.06	0.0	0	0.09	0.0	0	0.25	0.0
Larynx	0	0.17	0.0	1	0.54	1.9	0	0.44	0.0	0	0.69	0.0	1	1.84	0.5
Trachea, bronchus, lung	2	1.31	1.5	5	4.25	1.2	5	3.56	1.4	8	6.14	1.3	20	15.25	1.3
Female breast	0	0.97	0.0	4	3.15	1.3	2	2.72	0.7	7	5.96	1.2	13	12.79	1.0
Female genital tract	**2**	**0.64**	**3.1**	**1**	**2.07**	**0.5**	**2**	**1.73**	**1.2**	**7**	**3.53**	**2.0**	**12**	**7.97**	**1.5**
Cervix uteri	1	0.15	6.7	0	0.49	0.0	1	0.40	2.5	0	0.66	0.0	2	1.70	1.2
Corpus uteri	1	0.23	4.4	0	0.74	0.0	1	0.65	1.5	5	1.52	3.3[b]	7	3.13	2.2
Uterus, NOS	0	0.06	0.0	0	0.17	0.0	0	0.12	0.0	0	0.16	0.0	0	0.51	0.0
Ovary, fallopian tubes	0	0.17	0.0	1	0.56	1.8	0	0.48	0.0	2	0.99	2.0	3	2.19	1.4
Prostate gland	6	1.28	4.7[b]	5	4.10	1.2	4	3.48	1.1	7	5.13	1.4	22	13.98	1.6
Testis	0	0.02	0.0	0	0.07	0.0	0	0.05	0.0	0	0.09	0.0	0	0.24	0.0
Kidney, renal pelvis, ureter	0	0.23	0.0	1	0.73	1.4	0	0.61	0.0	1	1.04	1.0	2	2.60	0.8
Bladder, other urinary	0	0.60	0.0	4	1.91	2.1	2	1.61	1.2	5	2.66	1.9	11	6.78	1.6
Melanoma of the skin	0	0.12	0.0	1	0.41	2.4	0	0.35	0.0	2	0.65	3.1	3	1.53	2.0
Eye	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.07	0.0	0	0.19	0.0
Brain, central nervous system	0	0.11	0.0	0	0.38	0.0	0	0.31	0.0	0	0.54	0.0	0	1.35	0.0
Thyroid gland	0	0.05	0.0	0	0.17	0.0	0	0.15	0.0	0	0.27	0.0	0	0.64	0.0
Bone	0	0.02	0.0	2	0.06	32.1[b]	0	0.05	0.0	1	0.07	14.9	3	0.20	15.4[b]
Connective tissue	1	0.06	16.4	1	0.18	5.4	0	0.14	0.0	2	0.24	8.3	4	0.63	6.3[b]
Lymphatic, hematopoietic system	**4**	**0.71**	**5.6**[b]	**1**	**2.28**	**0.4**	**2**	**1.92**	**1.0**	**2**	**3.42**	**0.6**	**9**	**8.33**	**1.1**
Non-Hodgkin's lymphoma	0	0.23	0.0	0	0.76	0.0	1	0.64	1.6	0	1.18	0.0	1	2.81	0.4
Hodgkin's disease	1	0.06	15.6	0	0.21	0.0	0	0.17	0.0	0	0.27	0.0	1	0.72	1.4
Multiple myeloma	0	0.10	0.0	0	0.33	0.0	0	0.28	0.0	0	0.55	0.0	0	1.27	0.0
Leukemias	3	0.31	9.7[b]	1	0.98	1.0	1	0.83	1.2	2	1.42	1.4	7	3.53	2.0
Chronic lymphocytic	1	0.09	11.1	0	0.29	0.0	1	0.25	4.0	1	0.44	2.3	3	1.06	2.8
Acute nonlymphocytic	1	0.09	10.8	0	0.30	0.0	0	0.25	0.0	1	0.46	2.2	2	1.10	1.8

[a] ICD-O code = 171.

[b] $P < .05$.

CONNECTIVE TISSUE MALES

TABLE 6D. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the connective tissue among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,112			874			491			308			1,112		
Person-yr in interval	805			2,564			1,949			2,693			8,011		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**13**	**7.02**	**1.9**	**28**	**22.49**	**1.2**	**19**	**18.61**	**1.0**	**32**	**27.54**	**1.2**	**92**	**75.63**	**1.2**
All excluding site of initial cancer	**13**	**6.98**	**1.9**	**27**	**22.37**	**1.2**	**19**	**18.51**	**1.0**	**31**	**27.39**	**1.1**	**90**	**75.22**	**1.2**
Buccal cavity, pharynx	**0**	**0.36**	**0.0**	**0**	**1.17**	**0.0**	**1**	**0.95**	**1.0**	**1**	**1.34**	**0.7**	**2**	**3.82**	**0.5**
Lip	0	0.07	0.0	0	0.23	0.0	1	0.18	5.5	0	0.23	0.0	1	0.71	1.4
Tongue	0	0.07	0.0	0	0.23	0.0	0	0.19	0.0	1	0.26	3.8	1	0.75	1.3
Salivary gland	0	0.02	0.0	0	0.06	0.0	0	0.05	0.0	0	0.07	0.0	0	0.21	0.0
Gum, other mouth	0	0.10	0.0	0	0.32	0.0	0	0.26	0.0	0	0.38	0.0	0	1.06	0.0
Pharynx	0	0.09	0.0	0	0.28	0.0	0	0.23	0.0	0	0.34	0.0	0	0.94	0.0
Digestive system	**2**	**2.29**	**0.9**	**10**	**7.28**	**1.4**	**6**	**5.93**	**1.0**	**10**	**8.52**	**1.2**	**28**	**24.01**	**1.2**
Esophagus	0	0.15	0.0	0	0.48	0.0	0	0.39	0.0	0	0.55	0.0	0	1.57	0.0
Stomach	1	0.45	2.2	2	1.42	1.4	1	1.11	0.9	1	1.45	0.7	5	4.43	1.1
Colon	1	0.83	1.2	5	2.66	1.9	5	2.21	2.3	4	3.30	1.2	15	8.99	1.7
Rectum	0	0.47	0.0	1	1.50	0.7	0	1.21	0.0	2	1.75	1.1	3	4.94	0.6
Liver, biliary	0	0.12	0.0	0	0.36	0.0	0	0.30	0.0	0	0.44	0.0	0	1.22	0.0
Pancreas	0	0.23	0.0	1	0.73	1.4	0	0.60	0.0	3	0.89	3.4	4	2.44	1.6
Respiratory system	**1**	**1.32**	**0.8**	**6**	**4.28**	**1.4**	**4**	**3.56**	**1.1**	**7**	**5.52**	**1.3**	**18**	**14.67**	**1.2**
Nasal cavities, sinuses	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.06	0.0	0	0.17	0.0
Larynx	0	0.16	0.0	1	0.50	2.0	0	0.41	0.0	0	0.61	0.0	1	1.67	0.6
Trachea, bronchus, lung	1	1.14	0.9	5	3.69	1.4	4	3.08	1.3	7	4.81	1.5	17	12.70	1.3
Prostate gland	6	1.28	4.7[b]	5	4.10	1.2	4	3.48	1.1	7	5.13	1.4	22	13.98	1.6
Testis	0	0.02	0.0	0	0.07	0.0	0	0.05	0.0	0	0.09	0.0	0	0.24	0.0
Kidney, renal pelvis, ureter	0	0.17	0.0	1	0.55	1.8	0	0.46	0.0	0	0.69	0.0	1	1.87	0.5
Bladder, other urinary	0	0.50	0.0	3	1.61	1.9	2	1.35	1.5	3	2.04	1.5	8	5.49	1.5
Melanoma of the skin	0	0.08	0.0	1	0.26	3.8	0	0.22	0.0	0	0.35	0.0	1	0.91	1.1
Eye	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.04	0.0	0	0.11	0.0
Brain, central nervous system	0	0.08	0.0	0	0.25	0.0	0	0.20	0.0	0	0.31	0.0	0	0.83	0.0
Thyroid gland	0	0.02	0.0	0	0.07	0.0	0	0.05	0.0	0	0.09	0.0	0	0.23	0.0
Bone	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0
Connective tissue	0	0.04	0.0	1	0.12	8.0	0	0.10	0.0	1	0.15	6.8	2	0.41	4.9
Lymphatic, hematopoietic system	**4**	**0.48**	**8.4**[b]	**1**	**1.54**	**0.6**	**2**	**1.29**	**1.6**	**1**	**1.92**	**0.5**	**8**	**5.22**	**1.5**
Non-Hodgkin's lymphoma	0	0.15	0.0	0	0.48	0.0	1	0.41	2.5	0	0.62	0.0	1	1.66	0.6
Hodgkin's disease	1	0.04	23.6	0	0.14	0.0	0	0.11	0.0	0	0.16	0.0	1	0.45	2.2
Multiple myeloma	0	0.07	0.0	0	0.22	0.0	0	0.18	0.0	0	0.28	0.0	0	0.75	0.0
Leukemias	3	0.22	13.8[b]	1	0.70	1.4	1	0.58	1.7	1	0.86	1.2	6	2.36	2.5
Chronic lymphocytic	1	0.07	15.0	0	0.22	0.0	1	0.19	5.4	1	0.28	3.6	3	0.74	4.0
Acute nonlymphocytic	1	0.06	16.0	0	0.20	0.0	0	0.17	0.0	0	0.26	0.0	1	0.70	1.4

[a] ICD-O code = 171.

[b] $P < .05$.

CONNECTIVE TISSUE FEMALES

TABLE 6E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the connective tissue among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	885			709			411			289			885		
Person-yr in interval	641			2,088			1,718			2,924			7,371		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	5	3.73	1.3	15	11.88	1.3	8	9.96	0.8	32	22.18	1.4	60	47.72	1.3
All excluding site of initial cancer	4	3.71	1.1	15	11.82	1.3	8	9.91	0.8	31	22.09	1.4	58	47.50	1.2
Buccal cavity, pharynx	0	0.06	0.0	0	0.20	0.0	0	0.17	0.0	1	0.40	2.5	1	0.83	1.2
Lip	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	1	0.02	45.9	1	0.05	20.4
Tongue	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.08	0.0	0	0.17	0.0
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.05	0.0	0	0.11	0.0
Gum, other mouth	0	0.02	0.0	0	0.07	0.0	0	0.06	0.0	0	0.14	0.0	0	0.29	0.0
Pharynx	0	0.01	0.0	0	0.04	0.0	0	0.04	0.0	0	0.09	0.0	0	0.18	0.0
Digestive system	1	1.14	0.9	6	3.57	1.7	3	2.89	1.0	7	6.47	1.1	17	14.07	1.2
Esophagus	0	0.02	0.0	0	0.08	0.0	0	0.06	0.0	0	0.15	0.0	0	0.31	0.0
Stomach	0	0.16	0.0	0	0.51	0.0	2	0.38	5.2	2	0.73	2.7	4	1.79	2.2
Colon	0	0.53	0.0	4	1.64	2.4	1	1.36	0.7	4	3.14	1.3	9	6.66	1.4
Rectum	1	0.22	4.6	0	0.68	0.0	0	0.55	0.0	1	1.25	0.8	2	2.69	0.7
Liver, biliary	0	0.08	0.0	0	0.25	0.0	0	0.19	0.0	0	0.41	0.0	0	0.93	0.0
Pancreas	0	0.11	0.0	1	0.34	2.9	0	0.28	0.0	0	0.68	0.0	1	1.41	0.7
Respiratory system	1	0.19	5.1	0	0.63	0.0	1	0.54	1.9	1	1.47	0.7	3	2.83	1.1
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.08	0.0
Larynx	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.09	0.0	0	0.17	0.0
Trachea, bronchus, lung	1	0.17	5.8	0	0.56	0.0	1	0.48	2.1	1	1.33	0.8	3	2.54	1.2
Female breast	0	0.97	0.0	4	3.15	1.3	2	2.72	0.7	7	5.96	1.2	13	12.79	1.0
Female genital tract	2	0.64	3.1	1	2.07	0.5	2	1.73	1.2	7	3.53	2.0	12	7.97	1.5
Cervix uteri	1	0.15	6.7	0	0.49	0.0	1	0.40	2.5	0	0.66	0.0	2	1.70	1.2
Corpus uteri	1	0.23	4.4	0	0.74	0.0	1	0.65	1.5	5	1.52	3.3^b	7	3.13	2.2
Uterus, NOS	0	0.06	0.0	0	0.17	0.0	0	0.12	0.0	0	0.16	0.0	0	0.51	0.0
Ovary, fallopian tubes	0	0.17	0.0	1	0.56	1.8	0	0.48	0.0	2	0.99	2.0	3	2.19	1.4
Kidney, renal pelvis, ureter	0	0.06	0.0	0	0.18	0.0	0	0.15	0.0	1	0.34	2.9	1	0.73	1.4
Bladder, other urinary	0	0.10	0.0	1	0.31	3.2	0	0.26	0.0	2	0.62	3.2	3	1.29	2.3
Melanoma of the skin	0	0.04	0.0	0	0.15	0.0	0	0.13	0.0	2	0.29	6.8	2	0.62	3.2
Eye	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.08	0.0
Brain, central nervous system	0	0.04	0.0	0	0.13	0.0	0	0.11	0.0	0	0.24	0.0	0	0.52	0.0
Thyroid gland	0	0.03	0.0	0	0.11	0.0	0	0.09	0.0	0	0.18	0.0	0	0.41	0.0
Bone	0	0.01	0.0	2	0.02	89.3^b	0	0.02	0.0	1	0.03	35.3	3	0.07	40.4^b
Connective tissue	1	0.02	50.1	0	0.06	0.0	0	0.05	0.0	1	0.09	10.6	2	0.22	9.0^b
Lymphatic, hematopoietic system	0	0.23	0.0	0	0.74	0.0	0	0.64	0.0	1	1.50	0.7	1	3.11	0.3
Non-Hodgkin's lymphoma	0	0.08	0.0	0	0.27	0.0	0	0.23	0.0	0	0.56	0.0	0	1.15	0.0
Hodgkin's disease	0	0.02	0.0	0	0.07	0.0	0	0.06	0.0	0	0.11	0.0	0	0.27	0.0
Multiple myeloma	0	0.04	0.0	0	0.11	0.0	0	0.10	0.0	0	0.27	0.0	0	0.52	0.0
Leukemias	0	0.09	0.0	0	0.29	0.0	0	0.24	0.0	1	0.55	1.8	1	1.17	0.9
Chronic lymphocytic	0	0.02	0.0	0	0.07	0.0	0	0.06	0.0	0	0.16	0.0	0	0.32	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.09	0.0	0	0.08	0.0	1	0.20	5.1	1	0.40	2.5

[a] ICD-O code = 171.

[b] $P < .05$.

Second Cancer Following Lymphatic and Hematopoietic Cancers in Connecticut, 1935–82 [1]

Mark H. Greene[2] *and* Jerome Wilson[3]

ABSTRACT—The risk of developing a second primary cancer was evaluated in approximately 19,000 persons with initial cancers of the lymphatic and hematopoietic system in Connecticut between 1935 and 1982. Significant excesses for all second cancers were observed among patients with leukemia (34%), Hodgkin's disease (70%), non-Hodgkin's lymphoma (25%), and multiple myeloma (24%). In general, the risk of second cancers was greater in males than in females, even for cohorts not showing an excess of surveillance-related prostate cancer. Among patients with leukemia, significant excesses of cancers of the lung, kidney/ureter, and prostate were noted; cutaneous melanoma was elevated only in males. These excesses did not persist in the small number of long-term survivors. Possible etiologic factors included tobacco smoking for lung and kidney cancers, medical surveillance artifact for prostate cancer, and immunosuppression for malignant melanoma and lung cancer. The large number and good prognoses of patients with chronic lymphocytic leukemia strongly influenced the pattern of second cancers when all leukemias were analyzed together; no evidence was found for an increased risk of second cancer in patients with acute lymphocytic leukemia. A disproportionate number of subsequent cancers, particularly those of the kidney and ureter, were diagnosed incidentally at autopsy. Patients with Hodgkin's disease displayed significant excesses of cancers of the buccal cavity and pharynx, lung, female breast, and thyroid. The latter 3 sites remained significantly elevated in long-term survivors (10 yr or more postdiagnosis), so that radiation therapy may have contributed to their development. Among persons with non-Hodgkin's lymphoma, cancers of the stomach, lung, brain, and connective tissue occurred excessively. The first 3 sites, plus cancers of the urinary bladder, remained elevated among long-term survivors. The brain cancer excess, not previously reported, may represent misclassification of central nervous system lymphoma. The risk of gastric cancer is reminiscent of similar findings in patients with both acquired and genetically determined immunodeficiency disorders. The alkylating agent, cyclophosphamide, used extensively in the treatment of non-Hodgkin's lymphoma, is known to cause bladder cancer in man. The only significant excess observed in patients with multiple myeloma was acute nonlymphocytic leukemia (in both sexes), a well-known complication of alkylating agent chemotherapy; this excess was demonstrated despite past tumor registry coding practices which diminished the likelihood of leukemia being classified as an independent second cancer in patients whose index cancer was a leukemia or lymphoma. Analytic epidemiologic studies are needed if we are to clarify the contributions of host susceptibility, smoking, immune dysfunction, and various forms of anticancer therapy to the specific second cancer excesses observed in persons with lymphoid and hematopoietic cancer.—Natl Cancer Inst Monogr 68:191-217, 1985.

LEUKEMIA (ICD-O, M-9800–9940)

The leukemias are a heterogeneous group of cancers that comprise about 3% of all new cancers occurring in the United States (roughly equivalent proportions in both males and females) and 3.7% of all cancer deaths (*1*). These tumors are classified according to cell of origin (e.g., lymphocytic, granulocytic) and tempo of untreated disease (e.g., acute, chronic). The etiology of most leukemias remains obscure (*2*). Genetic factors contribute in some measure, as indicated by racial differences in susceptibility for various cell types, the occurrence of familial aggregations of leukemia, particularly CLL (*3*), and the presence of subtype-specific cytogenetic abnormalities (*4*). Excesses of each subtype except CLL have been described after people were exposed to ionizing radiation (*5*), whereas ANLL has been found excessive following exposure to occupational chemicals (e.g., benzene) and to therapeutic drugs, particularly alkylating agents (*6*). Recently, a newly identified class of retroviruses has been implicated as a cause of certain leukemias and lymphomas of T-cell origin (*7*). The prognosis for patients with leukemia has generally improved over the interval 1960–63 to 1970–73, with respective 5-year survival rates for white males by cell type being: 4 to 27% for ALL; 29 to 46% for CLL; 2 to 3% for acute granulocytic leukemia; and 13 to 18% for chronic granulocytic leukemia. The pattern is similar for white females (*8*). Chemotherapy, either as a single or multiple agent, comprises the mainstay of therapy for the leukemias and with improvements in the management of infectious and hemorrhagic complications accounts for the increases in survival. Radiation therapy is seldom given in the management of these patients.

In an earlier survey of multiple primary malignant tumors in Connecticut (*9*), patients with an index leukemia showed an increase in cancers of the liver and biliary tract, kidney and ureters (males only), and lung (statistically not

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ABBREVIATIONS: ICD-O = International Classification of Diseases for Oncology; CLL = chronic lymphocytic leukemia; ANLL = acute nonlymphocytic leukemia; ALL = acute lymphocytic leukemia; SEER = Surveillance, Epidemiologic and End Results (Program); RR = relative risk(s); CI = confidence interval; NHL = non-Hodgkin's lymphoma.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Environmental Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3C29, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Mark H. Greene, M.D.

[3] Radiation Epidemiology Branch, Division of Cancer Etiology.

significant). A recent literature review identified 61 patients with second cancers following ALL; though these data are nonquantitative, histiocytic medullary reticulosis, Hodgkin's disease, chronic myelogenous leukemia, and ANLL were suggested to comprise a disproportionately high number of second cancers (*10*). Of the leukemias, CLL appears to be the only specific one for which quantitative data on the risk of subsequent cancers are available. In an analysis of data collected by the National Cancer Institute's End Results Program (the predecessor to the SEER Program, which includes the Connecticut Tumor Registry), significant excesses of malignant melanoma, soft tissue sarcomas, and lung cancers were observed among 4,869 patients with CLL (*11*). The pattern of cancer excesses in this study suggested a role for leukemia-related immunosuppression rather than leukemia therapy in the genesis of these subsequent cancers.

Results

Between 1935 and 1982, a total of 6,727 persons developed leukemia in Connecticut. The average age at diagnosis was 53 years, and the average follow-up was 2.6 years. The mean year of diagnosis was 1966. Males were 36% more likely to develop leukemia than were females, and only 19% of these patients received radiation therapy as part of their initial treatment. Overall, 264 (or 3.9%) of them developed a second cancer, compared with 198 expected on the basis of rates in the general population (RR = 1.33; 95% CI = 1.2–1.5). Cancers of the digestive ($n = 90$), genitourinary ($n = 70$) and respiratory ($n = 57$) tracts accounted for 82% of all second tumors. Significant excesses were found for cancers of the lung (RR = 2.1; 95% CI = 1.5–2.7), prostate (RR = 1.7; 95% CI = 1.2–2.2), and kidney/ureter (RR = 3.1; 95% CI = 1.6–5.2). Sites that were elevated, but not significantly, included cancers of the buccal cavity (particularly tongue), colon, rectum, pancreas, connective tissue, and malignant melanoma. The risk of developing a second cancer was higher in men (RR = 1.4) than in women (1.2). The excess risks of lung and kidney cancers were of similar magnitude in both sexes but achieved statistical significance only in males. The melanoma excess was seen in males only. Cancers of the female genital tract and lymphatic and hematopoietic system occurred significantly below expectation.

An excess of second cancers was not observed among the 318 persons surviving 10 or more years after the initial diagnosis of leukemia (RR = 0.9). The lung cancer risk was significantly elevated through 9 years of follow-up, with a smaller (nonsignificant) excess at or beyond 10 years in both sexes (RR = 1.5, males; 2.5, females). No kidney/ureter cancers were observed beyond 10 years of follow-up; the excess at this site was most striking among the men who, during the first year after leukemia was diagnosed, developed 7 of the 13 cancers of the kidney (RR = 11). The excess risk of prostate cancer was observed only during the first 4 years of follow-up. Two of the 5 melanomas occurred after 10 years of follow-up (RR = 9.1; 95% CI = 1.0–33.0).

Discussion

Persons with leukemia showed a significant 34% increased risk of developing a second cancer throughout subsequent years of survival. The excess risk of prostate cancer declined substantially over time, which may reflect a medical surveillance bias, with enhanced detection of a common tumor that often remains clinically silent. A lung cancer excess appeared early and persisted in both sexes throughout follow-up, with a similar pattern for cancers of the kidney/ureter. The risk of kidney/ureter cancer as a function of time since initial diagnosis of leukemia followed an erratic pattern that might partly have been a consequence of the relatively small number of cases. The presence of a large risk of these solid tumors within the first year of follow-up argues against a role for leukemia therapy in their pathogenesis and suggests some risk factors in common with the leukemias. An excess risk of lung cancer has been reported following Hodgkin's disease and non-Hodgkin's lymphoma (*12*), and an excess risk of leukemia has been seen following renal cancer (*13*). The possibility that tobacco smoking may be important in the excesses of lung and kidney cancer gains some support from the presence of an excess (nonsignificant) of cancers of the buccal cavity; recent data suggest that smoking may be a risk factor for leukemia (Winn DM: Unpublished data).

One difficulty in assessment of the magnitude of the kidney cancer excess is the fact that 7 of 13 cancers were diagnosed incidentally at autopsy (data not shown). Because patients with leukemia are much more likely to undergo autopsy than are other cancer patients or persons in the general population, this aggressive case-finding may artificially inflate the relative risks of secondary kidney cancer. Nonetheless, cancers of this site are, unlike prostate cancer, uncommon and do not frequently remain clinically occult. Although the magnitude of the risk of kidney/ureter cancer in leukemia patients may be uncertain, the association itself is likely to be real and of some unknown biologic significance. The high frequency of autopsies in patients with leukemia contributes substantially to the excess risks observed in this series. If one deletes from consideration those subsequent cancers diagnosed only at autopsy, the number of second cancers in the leukemia cohort would be decreased from 264 to 218 (RR = 1.1 for all sites combined). The excess of prostate cancer disappears completely (RR = 1.0), whereas that for kidney/ureter decreases to nonsignificant levels (RR = 1.4). Strictly speaking, the expected values should also be reduced to remove the contribution of autopsy finding to incidence rates in the general population. However, the excess risk of lung cancer persists (RR = 1.7; 95% CI = 1.2–2.2) and suggests that this site is the single most important cancer which occurs subsequent to leukemia. The excess risk of malignant melanoma was also unaffected by the elimination of cancers diagnosed at autopsy. Although based on small numbers and confined to males, this excess is consistent with previous reports that indicate an association between immunosuppression and melanoma pathogenesis (*11, 14, 15*). Lung cancer may also be related to immunosuppression, as in kidney transplant recipients (*16*).

Although logistic considerations dictated that we analyze and report the leukemias as a group, this approach does obscure some important information that can only be appreciated by considering the major leukemia types separately. For example, CLL patterns dominate these data. Whereas CLL contributes 1,875 patients, 28% of all leukemias, to the total cohort, it accounts for 47% of the total person-years of observation due to the longer survival (mean follow-up: 4.4 years). Similarly, 165 patients with CLL developed second cancers (RR = 1.3; 95% CI = 1.1–1.5), 63% of the total experience of all leukemia patients combined. Furthermore, the excesses of cancers of the lung (n = 34; RR = 2.0; 95% CI = 1.4–2.8), prostate (n = 22; RR = 1.3; 95% CI = 0.8–2.0), kidney/ureter (n = 8; RR = 3.0; 95% CI = 1.3–5.9), and cutaneous melanoma (n = 4; RR = 3.1; 95% CI = 0.8–8.0) are derived from the subset of patients with CLL. The pattern of excess second cancers is similar among patients with acute granulocytic and chronic granulocytic leukemia, but only 5 second cancers occurred in patients with ALL in our series, and only 4 second cancers were previously reported in a study of 1,530 long-term survivors with this disease (*17*). These findings suggest that the substantial improvements in survival that have occurred in ALL do not seem to have brought with them a dramatic excess of treatment-related second cancers, at least none that can be detected with the number of patients and duration of follow-up available in the current cohort. However, the reader should note that past reporting practices in Connecticut prevent an assessment of the risk of ANLL, the most well-documented chemotherapy-related second cancer, in patients whose index disease is a leukemia of a different cell type (*13*). This important association must be addressed by alternative analytic approaches.

HODGKIN'S DISEASE (ICD-O, M-9650–9662)

Hodgkin's disease, which comprises approximately 0.8% of all new cancers occurring in the United States, is more common in men (1.0%) than in women (0.7%). The overall mortality from Hodgkin's disease is relatively low and currently accounts for about 0.3% of all cancer deaths in the United States (*1*). One of the salient epidemiologic features of Hodgkin's disease is its trimodal age distribution, which has suggested to us that this diagnostic rubric may include at least 3 distinctive diseases (*18*). Familial and geographic clustering of Hodgkin's disease has been studied extensively; this phenomenon, in conjunction with strong social class and behavioral correlates of disease risk, has led to the hypothesis that the young adult variety of Hodgkin's disease represents an uncommon consequence of exposure to a widely prevalent transmissible agent, probably a virus, with age at exposure a critical determinant of outcome (*18*). Hodgkin's disease has not been linked to ionizing radiation exposure (*5*), whereas various occupational exposures, particularly woodworking, have been implicated but not yet proved as etiologically important (*18*). The application of megavoltage nodal irradiation or combination chemotherapy regimens, or both, has resulted in dramatic improvements in survival and cure rates even for patients who present with advanced disease (*19*). In a comparison of rates for 1960–63 with 1970–73, the 5-year survival rates for white males have nearly doubled, 34 to 66%, with a similar pattern among white females, 48 to 69% (*8*).

In an earlier study of multiple primary cancers in Connecticut during 1935–64, patients with Hodgkin's disease were considered in combination with those having other malignant lymphomas (*9*). However, Hodgkin's disease has been subjected to epidemiologic analyses of subsequent cancer risk that far exceed those for any other human cancer, resulting in a literature much too extensive to cite in the present context (*20*). In summary, patients with Hodgkin's disease experience a dramatic excess of ANLL (and pre-leukemia), the bulk of which is a consequence of exposure to aggressive chemotherapy which includes one or more alkylating agents (*21–25*). The addition of radiation therapy to chemotherapy may increase the risk of ANLL still further, but radiation therapy alone rarely eventuates in leukemia. A similar pattern of excess risk for subsequent NHL has emerged recently (*22*). It is not yet clear whether patients with Hodgkin's disease are at increased risk of subsequent sarcoma or carcinoma, although the available data suggest that such excesses will be found as larger numbers of patients are followed for longer periods and that radiation therapy is likely to play a more significant role in their pathogenesis. A recent report has documented an excess of malignant melanoma in patients with Hodgkin's disease (*15*). These second cancers arose from preexisting melanoma precursors (dysplastic nevi) in a setting of compromised immune function.

Results

Between 1935 and 1982, of the 3,211 persons who developed Hodgkin's disease in Connecticut, the average age at diagnosis was 40 years, and the mean duration of follow-up was 5.0 years. The average year of diagnosis was 1965. Males were 31% more likely to develop Hodgkin's disease than were females. Nearly 66% of these patients received radiation therapy as part of their initial treatment. Overall, 97 (or 3.0%) of the patients with Hodgkin's disease developed a second cancer, compared with 57 expected based on rates in the general population (RR = 1.70; 95% CI = 1.4–2.1).

Cancers of the lung (n = 23), female breast (n = 15), gastrointestinal tract (n = 13), and buccal cavity (n = 7) accounted for 60% of all second cancer. Overall, significant excesses were seen for cancers of the buccal cavity and pharynx (RR = 3.1; 95% CI = 1.3–6.4), lung (RR = 3.1; 95% CI = 2.0–4.7), female breast (RR = 1.9; 95% CI = 1.1–3.1), and thyroid (RR = 6.7; 95% CI = 1.8–17.1). Sites that were elevated, but not significantly, included cancers of the liver and biliary ducts, urinary bladder, bone and connective tissue, NHL, and ANLL. The risk of a second cancer developing was slightly higher in males (RR = 1.8) than in females (1.5). The excesses of cancers of the buccal cavity and bladder and NHL were seen primarily in males, whereas the excess of thyroid cancer was confined to females.

Excess second cancers have persisted among the 516 persons surviving 10 and more years after the initial diagnosis of Hodgkin's disease (RR = 2.0; 95% CI = 1.3–2.8) in both men (RR = 1.4) and women (RR = 2.5). This group of long-term survivors experienced significantly high risks for cancers of the lung (RR = 5.5), breast (3.0), and thyroid (13). Overall, the risk of second cancers by interval after diagnosis of Hodgkin's disease showed modest (nonsignificant) excesses during the first 4 years of follow-up and significant excesses thereafter. Risk appeared to increase with time since diagnosis for all sites combined, and for cancers of the lung, breast, and thyroid. The risks of these latter cancers were all greatest at or beyond 10 years of follow-up.

Discussion

Persons with Hodgkin's disease showed a significant 70% increased risk of developing a second cancer throughout subsequent years of observation. Significant excesses of ANLL and NHL, the 2 best characterized post-Hodgkin's disease cancers, were not observed in these data. This finding was not unexpected, inasmuch as past tumor registry coding practices reduced the likelihood of recording either of these 2 cancers as independent primary tumors following an index case of Hodgkin's disease (*13*). However, nonsignificant excesses of both ANLL and NHL were observed despite these methodologic difficulties. The most significant excesses observed were for cancers of the buccal cavity and lung in men, and cancers of the lung, breast, and thyroid in women. With the exception of the buccal cavity tumors, the excesses at the remaining 3 sites rose as duration of follow-up increased and reached a maximum at the longest follow-up interval. All 3 sites are known to be radiation-related cancers (*5*), particularly the breast and thyroid. Although detailed exposure data are not available, the fact that the highest risks occurred at or beyond 10 years is consistent with the known relatively long latent period of radiogenic solid tumors. The excesses of bone and connective tissue tumors, though based on small numbers, might be attributable to radiation as well. The excess risks of buccal cavity, lung, and bladder cancers in men raises the possibility that smoking was a factor in the pathogenesis of these second tumors. Alkylating agents, especially cyclophosphamide, used extensively in the management of Hodgkin's disease, have been implicated as a cause of bladder cancer (*26, 27*). No excess of prostate cancer was observed following Hodgkin's disease (in contrast with most other index cancers), perhaps due to the relatively young age of the person at its onset.

NON-HODGKIN'S LYMPHOMA (ICD-O, M-9590–9642, 9690–9701, 9750)

The incidence rates of NHL, malignant lymphomas which lack the Reed-Sternberg cell characteristic of Hodgkin's disease, are 5.7 and 8.1 per 100,000 per year for females and males, respectively (*28*). The histologic classification of NHL has evolved over the past 20 years, and little epidemiologic information is available on the various entities which comprise this category; thus the causes of most lymphomas are largely unknown. Genetic factors may be implicated because numerous familial aggregations of NHL have been reported (*29*). Immune dysfunction, both therapeutically and genetically induced, has been shown to increase greatly the risk of NHL (*16, 29, 30*), whereas exposure to ionizing radiation results in more modest excesses (*29*), if any (*31*). The 5-year survival rate has increased between 1960–63 and 1970–73 from 31 to 39% for men and from 31 to 43% for women (*8*).

Several reports have suggested possible relationships between NHL and the development of a second cancer (*12, 32*). In an earlier evaluation of the Connecticut data, Schoenberg (*9*) found significant elevations for cancers of the pharynx, lung, cervix, and prostate. These data are difficult for us to interpret because the analysis considered all malignant lymphomas as a single group. Workers at the National Cancer Institute reported that patients experienced a high risk of developing ANLL (*12*).

Results

There were 6,734 persons who developed NHL in Connecticut between 1935 and 1982. The average age at diagnosis was 58 years, and the average follow-up was 4 years. The average year of diagnosis was 1967. About 51% of the population received radiation treatment for the first primary cancer. Overall, 319 persons (or 4.7%) developed a second cancer, compared with 256 expected on the basis of general population rates (RR = 1.24; 95% CI = 1.11–1.39). Lung cancer accounted for 20% of all second primary cancers (RR = 1.9; 95% CI = 1.4–2.4). Significant excesses were also found for cancers of the stomach (RR = 1.7; 95% CI = 1.1–2.7), brain (RR = 3.1; 95% CI = 1.4–5.8), and connective tissue (RR = 5.0; 95% CI = 1.8–10.8). Sites that were elevated in both sexes, but not significantly, included cancers of the liver/biliary tract, pancreas, urinary bladder, and thyroid. Males (RR = 1.3) were slightly more likely to develop second cancers than were females (RR = 1.1) and also had nonsignificant excesses of cancer of the lip, tongue, larynx, and ANLL. The highest risk of a second cancer developing among males was seen during the first year after diagnosis, with the excess largely attributable to cancers of the prostate, lung, and digestive organs.

The risk of a second cancer developing was significantly elevated in all follow-up intervals except 1–4 years since initial diagnosis, which suggested that the diagnoses of some second cancers have been advanced in time due to increased medical surveillance. Among 796 persons who were followed 10 or more years from their initial diagnosis, 76 (or 9.5%) developed a second primary (RR = 1.3; 95% CI = 1.0–1.6). Cancers of the stomach (RR = 2.8) and bladder (RR = 2.4) were significantly excessive in 10-year survivors, whereas cancers of the lung (RR = 1.6) and brain (RR = 4.6) were elevated but not significantly.

Discussion

A significant 24% excess of a second cancer developing following NHL was observed. The significant 73% excess of stomach cancer is noteworthy because previous evidence of an association between NHL and gastric cancer is limited to case reports (*33*). Gastric cancer may be induced by ionizing radiation (*5*), and the nodal irradiation administered to patients with NHL often encompasses the stomach. Alternatively, gastric cancer has also been observed in immunologically compromised patients (*16, 29*), and NHL patients have diminished immune function, both intrinsically and as a consequence of cytotoxic therapy (*34*). Lung cancer showed a significant excess and nonsignificant elevations for cancers of the lip, larynx, pancreas, and bladder, a pattern of tumor suggestive of an etiologic role for smoking. Whereas most previous reports noted a disproportionate number of adenocarcinomas among the excess lung cancers, this was not found in our series. The high risk of connective tissue cancer might be due to radiation therapy (*35*). The excess risk of malignant melanoma was confined to males. Although based on 6 cases, this excess is consistent with previous reports that indicated an association between immunosuppression and melanoma development (*11, 15*). With the exception of lung and stomach cancers, the significant results were based on small numbers.

The risk of developing a second primary cancer remained significantly elevated among long-term survivors. The most unusual observation was the increased risk of brain cancer, a result not previously reported in studies of second primaries following NHL. Of the 9 cases, 7 were histologically classified as gliomas. Although this excess is significant, it is possible that some are brain lymphomas (so-called "microgliomas" in older terminology), and, if so, the tumors should not be considered second primaries. The elevated prostate cancer risk observed among men during the first year of follow-up is most likely an artifact of intensive medical surveillance. Among 372 females surviving 10 or more years, a significant risk of bladder cancer was found. Because cyclophosphamide (a central component of lymphoma chemotherapy) is a known cause of bladder cancer in humans, this risk is worth noting, even though based on only 4 cases (*27, 36*). In the past, tumor registry coding practices made it unlikely that ANLL would be recorded as a separate independent primary tumor when the index cancer was a malignant lymphoma (*13*). Nonetheless, a nonsignificant increased risk of ANLL was observed; this type of leukemia has been shown to occur excessively following combined modality therapy for NHL (*12*). The pattern of increased risk for malignant melanoma, soft tissue sarcoma, and lung cancer that was seen in this series resembles that reported among patients with CLL (*11*), a neoplasm closely related to NHL.

MULTIPLE MYELOMA (ICD-O, M-9730–9731)

Multiple myeloma is a plasma cell neoplasm that accounts for 1.1 and 2.1% of all cancers among whites and blacks, respectively, in the United States, with the highest reported incidence in the world among black males (*37*). Multiple myeloma may be induced by ionizing radiation (*5*), and occupational risks have been suggested among farmers, woodworkers, and those who work in the nuclear and petroleum industries (*38, 39*). Multiple myeloma represents one of the few cancers with which a more favorable survival is experienced by blacks than by whites. The 5-year survival rate is 22% for black males versus 21% for white males, and 18% for black females versus 17% for white females for the period 1964–73 (*8, 40*). The reasons for this difference in survival are unknown.

Results

Between 1935 and 1982, a total of 2,249 persons developed multiple myeloma in Connecticut. The average age at diagnosis was 65 years, and the average follow-up was 2 years. The average year of diagnosis was 1969. Only 38% of the patients initially were treated with radiation. Overall, 73 (or 3.2%) of the multiple myeloma patients developed a second cancer compared with 59 expected on the basis of rates in the general population of Connecticut (RR = 1.24; 95% CI = 0.97–1.55).

Cancers of the digestive, respiratory, lymphatic, and hematopoietic systems accounted for 62% of all second neoplasms. The only significant excess was for ANLL (RR = 16; 95% CI = 7.3–30.5), an increase that was significant in both males (RR = 13) and females (RR = 21). Sites that were elevated but not significantly included cancers of the stomach and prostate. Men were more likely to develop a second cancer (RR = 1.4) than were women (RR = 1.1). No site showed a significant deficit, nor was a significant excess of second cancers observed among the 43 persons surviving 10 or more years after the initial diagnosis of multiple myeloma. Overall, the pattern of second cancer occurrence did not vary over time since first diagnosis. The risk of developing ANLL was observed only during years 1–9 of follow-up.

Discussion

Persons with multiple myeloma showed a 24% increased risk of developing a second cancer throughout subsequent years of survival. Because of unfavorable survival rates for multiple myeloma, the average follow-up was only 2 years, and only 43 (or 2%) persons were followed 10 or more years. The only significant excess noted was for ANLL, which accounted for 1 in every 8 second cancers.

High rates of ANLL following multiple myeloma have been reported in several cohort studies (*41–46*). In 1 series, the cumulative risk of ANLL reached 17.4% at 50 months of follow-up (*42*) and was attributed to the leukemogenic effect of alkylating agent chemotherapy. The unusually high risk of leukemia following myeloma and the occasional occurrence of ANLL in untreated myeloma patients have indicated the presence of an intrinsic predisposition to ANLL among patients with multiple myeloma (*6*). Given that past tumor registry coding practices mitigate against recording ANLL as an independent second cancer in patients whose index cancer is multiple myeloma (*13*), the presence of a significant excess in both men and women is remarkable.

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NH LYMPHOMA
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial non-Hodgkin's lymphoma, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	3,539	3,195	6,734
No. who developed a second primary cancer	196	123	319
Average age at diagnosis of first cancer, yr	56	60	58
Average yr of diagnosis of first cancer	1966	1967	1967
Person-yr of follow-up	14,378	12,854	27,231
Average follow-up, yr	4.1	4.0	4.0
Percent given radiotherapy for first cancer	52.0	50.5	51.3

[a] ICD-O morphology codes = 9590–9642, 9690–9701, 9750.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial non-Hodgkin's lymphoma in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	285	89.4
Only the first cancer	26	8.2
Only the second cancer	7	2.2
Neither first nor second cancer	1	0.3
Total second primary cancers	319	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

NH LYMPHOMA
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial non-Hodgkin's lymphoma among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,734			4,363			1,814			796			6,734		
Person-yr in interval	4,333			11,097			6,006			5,795			27,231		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**62**	**40.47**	**1.5**[b]	**108**	**102.18**	**1.1**	**73**	**54.97**	**1.3**[b]	**76**	**58.86**	**1.3**[b]	**319**	**256.31**	**1.2**[b]
All excluding site of initial cancer	**61**	**39.49**	**1.5**[b]	**107**	**99.70**	**1.1**	**73**	**53.65**	**1.4**[b]	**73**	**57.45**	**1.3**	**314**	**250.12**	**1.3**[b]
Buccal cavity, pharynx	**2**	**1.50**	**1.3**	**5**	**3.77**	**1.3**	**2**	**2.04**	**1.0**	**1**	**2.16**	**0.5**	**10**	**9.46**	**1.1**
Lip	1	0.22	4.6	1	0.53	1.9	1	0.28	3.5	1	0.30	3.3	4	1.33	3.0
Tongue	0	0.30	0.0	2	0.75	2.7	1	0.41	2.4	0	0.43	0.0	3	1.89	1.6
Salivary gland	0	0.10	0.0	0	0.24	0.0	0	0.13	0.0	0	0.15	0.0	0	0.62	0.0
Gum, other mouth	0	0.45	0.0	1	1.13	0.9	0	0.61	0.0	0	0.65	0.0	1	2.84	0.4
Pharynx	1	0.38	2.6	1	0.96	1.0	0	0.52	0.0	0	0.55	0.0	2	2.41	0.8
Digestive system	**18**	**12.45**	**1.4**	**31**	**31.05**	**1.0**	**18**	**16.68**	**1.1**	**26**	**17.68**	**1.5**	**93**	**77.81**	**1.2**
Esophagus	0	0.61	0.0	3	1.53	2.0	0	0.81	0.0	0	0.86	0.0	3	3.81	0.8
Stomach	3	1.91	1.6	6	4.64	1.3	4	2.50	1.6	7	2.53	2.8[b]	20	11.56	1.7[b]
Colon	7	5.20	1.3	13	13.04	1.0	8	6.99	1.1	9	7.56	1.2	37	32.77	1.1
Rectum	4	2.52	1.6	4	6.34	0.6	2	3.41	0.6	3	3.58	0.8	13	15.83	0.8
Liver, biliary	1	0.71	1.4	2	1.76	1.1	1	0.95	1.1	2	1.00	2.0	6	4.41	1.4
Pancreas	3	1.27	2.4	3	3.19	0.9	3	1.72	1.7	3	1.85	1.6	12	8.03	1.5
Respiratory system	**14**	**6.04**	**2.3**[b]	**25**	**15.47**	**1.6**[b]	**20**	**8.27**	**2.4**[b]	**14**	**9.25**	**1.5**	**73**	**38.99**	**1.9**[b]
Nasal cavities, sinuses	0	0.08	0.0	0	0.20	0.0	0	0.11	0.0	0	0.11	0.0	0	0.49	0.0
Larynx	2	0.62	3.2	4	1.58	2.5	1	0.86	1.2	0	0.91	0.0	7	3.97	1.8
Trachea, bronchus, lung	12	5.28	2.3[b]	21	13.54	1.6	18	7.22	2.5[b]	13	8.14	1.6	64	34.16	1.9[b]
Female breast	1	4.59	0.2	6	11.78	0.5	6	6.36	0.9	7	6.02	1.2	20	28.73	0.7
Female genital tract	**2**	**2.81**	**0.7**	**5**	**7.13**	**0.7**	**3**	**3.85**	**0.8**	**3**	**3.49**	**0.9**	**13**	**17.26**	**0.8**
Cervix uteri	1	0.52	1.9	1	1.30	0.8	1	0.69	1.4	1	0.59	1.7	4	3.10	1.3
Corpus uteri	1	1.19	0.8	4	3.08	1.3	1	1.68	0.6	1	1.56	0.6	7	7.50	0.9
Uterus, NOS	0	0.17	0.0	0	0.39	0.0	0	0.20	0.0	0	0.15	0.0	0	0.91	0.0
Ovary, fallopian tubes	0	0.77	0.0	0	1.96	0.0	1	1.06	0.9	1	0.97	1.0	2	4.77	0.4
Prostate gland	12	3.87	3.1[b]	7	9.65	0.7	6	5.22	1.1	5	6.55	0.8	30	25.28	1.2
Testis	1	0.06	16.3	1	0.16	6.1	0	0.09	0.0	0	0.10	0.0	2	0.41	4.9
Kidney, renal pelvis, ureter	2	0.87	2.3	0	2.22	0.0	1	1.19	0.8	2	1.29	1.5	5	5.58	0.9
Bladder, other urinary	0	2.14	0.0	7	5.41	1.3	5	2.91	1.7	8	3.35	2.4[b]	20	13.80	1.4
Melanoma of the skin	2	0.50	4.0	3	1.32	2.3	1	0.72	1.4	1	0.79	1.3	7	3.33	2.1
Eye	0	0.06	0.0	0	0.16	0.0	0	0.09	0.0	0	0.09	0.0	0	0.39	0.0
Brain, central nervous system	2	0.46	4.3	1	1.20	0.8	3	0.64	4.7	3	0.65	4.6	9	2.95	3.1[b]
Thyroid gland	1	0.20	5.1	1	0.51	2.0	1	0.28	3.6	1	0.28	3.6	4	1.26	3.2
Bone	0	0.06	0.0	0	0.15	0.0	1	0.08	12.8	0	0.08	0.0	1	0.36	2.8
Connective tissue	0	0.19	0.0	5	0.48	10.3[b]	0	0.26	0.0	1	0.28	3.6	6	1.21	5.0[b]
Lymphatic, hematopoietic system	**4**	**2.74**	**1.5**	**2**	**6.90**	**0.3**	**2**	**3.71**	**0.5**	**4**	**4.04**	**1.0**	**12**	**17.37**	**0.7**
Non-Hodgkin's lymphoma	1	0.98	1.0	1	2.48	0.4	0	1.32	0.0	3	1.41	2.1	5	6.19	0.8
Hodgkin's disease	0	0.21	0.0	0	0.54	0.0	1	0.29	3.4	0	0.29	0.0	1	1.33	0.8
Multiple myeloma	1	0.44	2.3	0	1.11	0.0	0	0.60	0.0	0	0.67	0.0	1	2.81	0.4
Leukemias	2	1.11	1.8	1	2.77	0.4	1	1.50	0.7	1	1.66	0.6	5	7.04	0.7
Chronic lymphocytic	0	0.34	0.0	0	0.86	0.0	0	0.47	0.0	0	0.53	0.0	0	2.19	0.0
Acute nonlymphocytic	2	0.35	5.7	1	0.89	1.1	1	0.48	2.1	0	0.55	0.0	4	2.28	1.8

[a] ICD-O morphology codes = 9590–9642, 9690–9701, 9750.

[b] $P < .05$.

NH LYMPHOMA
MALES

TABLE 1D. – *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial non-Hodgkin's lymphoma among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,539			2,269			945			424			3,539		
Person-yr in interval	2,255			5,781			3,115			3,226			14,378		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**45**	**22.79**	**2.0**[b]	**62**	**57.30**	**1.1**	**45**	**30.81**	**1.5**[b]	**44**	**36.05**	**1.2**	**196**	**146.85**	**1.3**[b]
All excluding site of initial cancer	**44**	**22.27**	**2.0**[b]	**62**	**55.98**	**1.1**	**45**	**30.11**	**1.5**[b]	**43**	**35.23**	**1.2**	**194**	**143.48**	**1.4**[b]
Buccal cavity, pharynx	**2**	**1.18**	**1.7**	**4**	**2.95**	**1.4**	**2**	**1.60**	**1.3**	**1**	**1.75**	**0.6**	**9**	**7.47**	**1.2**
Lip	1	0.20	5.0	1	0.48	2.1	1	0.26	3.9	1	0.28	3.6	4	1.22	3.3
Tongue	0	0.23	0.0	2	0.59	3.4	1	0.32	3.1	0	0.34	0.0	3	1.49	2.0
Salivary gland	0	0.06	0.0	0	0.15	0.0	0	0.08	0.0	0	0.10	0.0	0	0.39	0.0
Gum, other mouth	0	0.34	0.0	1	0.84	1.2	0	0.46	0.0	0	0.50	0.0	1	2.13	0.5
Pharynx	1	0.31	3.3	0	0.77	0.0	0	0.42	0.0	0	0.46	0.0	1	1.95	0.5
Digestive system	**13**	**7.11**	**1.8**	**14**	**17.74**	**0.8**	**9**	**9.54**	**0.9**	**13**	**10.91**	**1.2**	**49**	**45.28**	**1.1**
Esophagus	0	0.49	0.0	2	1.21	1.6	0	0.65	0.0	0	0.70	0.0	2	3.04	0.7
Stomach	2	1.26	1.6	2	3.07	0.7	3	1.66	1.8	4	1.78	2.2	11	7.77	1.4
Colon	5	2.65	1.9	4	6.66	0.6	3	3.58	0.8	5	4.26	1.2	17	17.14	1.0
Rectum	3	1.50	2.0	3	3.76	0.8	1	2.02	0.5	2	2.28	0.9	9	9.56	0.9
Liver, biliary	1	0.36	2.7	0	0.91	0.0	1	0.49	2.1	1	0.57	1.8	3	2.32	1.3
Pancreas	2	0.73	2.7	3	1.82	1.6	1	0.99	1.0	0	1.14	0.0	6	4.67	1.3
Respiratory system	**9**	**4.84**	**1.9**	**19**	**12.34**	**1.5**	**15**	**6.59**	**2.3**[b]	**13**	**7.63**	**1.7**	**56**	**31.37**	**1.8**[b]
Nasal cavities, sinuses	0	0.05	0.0	0	0.12	0.0	0	0.07	0.0	0	0.08	0.0	0	0.32	0.0
Larynx	1	0.55	1.8	4	1.40	2.9	1	0.76	1.3	0	0.82	0.0	6	3.53	1.7
Trachea, bronchus, lung	8	4.19	1.9	15	10.70	1.4	14	5.70	2.5[b]	12	6.66	1.8	49	27.24	1.8[b]
Prostate gland	12	3.87	3.1[b]	7	9.65	0.7	6	5.22	1.1	5	6.55	0.8	30	25.28	1.2
Testis	1	0.06	16.3	1	0.16	6.1	0	0.09	0.0	0	0.10	0.0	2	0.41	4.9
Kidney, renal pelvis, ureter	1	0.59	1.7	0	1.51	0.0	1	0.81	1.2	1	0.93	1.1	3	3.84	0.8
Bladder, other urinary	0	1.64	0.0	7	4.13	1.7	4	2.22	1.8	4	2.68	1.5	15	10.67	1.4
Melanoma of the skin	2	0.29	6.9	2	0.76	2.6	1	0.41	2.5	1	0.49	2.0	6	1.95	3.1[b]
Eye	0	0.03	0.0	0	0.09	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Brain, central nervous system	2	0.28	7.2	0	0.72	0.0	2	0.38	5.2	3	0.42	7.1[b]	7	1.80	3.9[b]
Thyroid gland	1	0.07	14.3	0	0.18	0.0	1	0.10	10.0	0	0.11	0.0	2	0.46	4.3
Bone	0	0.04	0.0	0	0.09	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Connective tissue	0	0.12	0.0	3	0.30	10.0[b]	0	0.16	0.0	1	0.19	5.4	4	0.76	5.3[b]
Lymphatic, hematopoietic system	**2**	**1.56**	**1.3**	**1**	**3.92**	**0.3**	**1**	**2.11**	**0.5**	**2**	**2.49**	**0.8**	**6**	**10.07**	**0.6**
Non-Hodgkin's lymphoma	1	0.52	1.9	0	1.32	0.0	0	0.70	0.0	1	0.82	1.2	2	3.37	0.6
Hodgkin's disease	0	0.13	0.0	0	0.33	0.0	0	0.18	0.0	0	0.19	0.0	0	0.82	0.0
Multiple myeloma	0	0.23	0.0	0	0.58	0.0	0	0.31	0.0	0	0.38	0.0	0	1.51	0.0
Leukemias	1	0.68	1.5	1	1.69	0.6	1	0.92	1.1	1	1.09	0.9	4	4.37	0.9
Chronic lymphocytic	0	0.22	0.0	0	0.54	0.0	0	0.30	0.0	0	0.36	0.0	0	1.41	0.0
Acute nonlymphocytic	1	0.20	4.9	1	0.51	1.9	1	0.27	3.6	0	0.34	0.0	3	1.33	2.3

[a] ICD-O morphology codes = 9590–9642, 9690–9701, 9750.

[b] $P < .05$.

NH LYMPHOMA FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial non-Hodgkin's lymphoma among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,195			2,094			869			372			3,195		
Person-yr in interval	2,077			5,317			2,891			2,569			12,854		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**17**	**17.68**	**1.0**	**46**	**44.88**	**1.0**	**28**	**24.16**	**1.2**	**32**	**22.81**	**1.4**	**123**	**109.46**	**1.1**
All excluding site of initial cancer	**17**	**17.23**	**1.0**	**45**	**43.73**	**1.0**	**28**	**23.54**	**1.2**	**30**	**22.22**	**1.4**	**120**	**106.65**	**1.1**
Buccal cavity, pharynx	**0**	**0.32**	**0.0**	**1**	**0.82**	**1.2**	**0**	**0.44**	**0.0**	**0**	**0.42**	**0.0**	**1**	**1.99**	**0.5**
Lip	0	0.02	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Tongue	0	0.06	0.0	0	0.17	0.0	0	0.09	0.0	0	0.09	0.0	0	0.40	0.0
Salivary gland	0	0.04	0.0	0	0.10	0.0	0	0.05	0.0	0	0.05	0.0	0	0.24	0.0
Gum, other mouth	0	0.11	0.0	0	0.29	0.0	0	0.15	0.0	0	0.15	0.0	0	0.70	0.0
Pharynx	0	0.07	0.0	1	0.19	5.3	0	0.10	0.0	0	0.09	0.0	1	0.45	2.2
Digestive system	**5**	**5.34**	**0.9**	**17**	**13.32**	**1.3**	**9**	**7.14**	**1.3**	**13**	**6.77**	**1.9**[b]	**44**	**32.53**	**1.4**
Esophagus	0	0.12	0.0	1	0.31	3.2	0	0.17	0.0	0	0.16	0.0	1	0.76	1.3
Stomach	1	0.65	1.6	4	1.57	2.6	1	0.84	1.2	3	0.75	4.0	9	3.80	2.4[b]
Colon	2	2.55	0.8	9	6.38	1.4	5	3.42	1.5	4	3.30	1.2	20	15.63	1.3
Rectum	1	1.02	1.0	1	2.57	0.4	1	1.38	0.7	1	1.30	0.8	4	6.27	0.6
Liver, biliary	0	0.35	0.0	2	0.86	2.3	0	0.46	0.0	1	0.43	2.3	3	2.09	1.4
Pancreas	1	0.54	1.8	0	1.37	0.0	2	0.73	2.7	3	0.71	4.2	6	3.36	1.8
Respiratory system	**5**	**1.20**	**4.2**[b]	**6**	**3.13**	**1.9**	**5**	**1.68**	**3.0**	**1**	**1.62**	**0.6**	**17**	**7.62**	**2.2**[b]
Nasal cavities, sinuses	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.18	0.0
Larynx	1	0.07	14.5	0	0.18	0.0	0	0.10	0.0	0	0.09	0.0	1	0.44	2.3
Trachea, bronchus, lung	4	1.09	3.7	6	2.84	2.1	4	1.52	2.6	1	1.47	0.7	15	6.92	2.2[b]
Female breast	1	4.59	0.2	6	11.78	0.5	6	6.36	0.9	7	6.02	1.2	20	28.73	0.7
Female genital tract	**2**	**2.81**	**0.7**	**5**	**7.13**	**0.7**	**3**	**3.85**	**0.8**	**3**	**3.49**	**0.9**	**13**	**17.26**	**0.8**
Cervix uteri	1	0.52	1.9	1	1.30	0.8	1	0.69	1.4	1	0.59	1.7	4	3.10	1.3
Corpus uteri	1	1.19	0.8	4	3.08	1.3	1	1.68	0.6	1	1.56	0.6	7	7.50	0.9
Uterus, NOS	0	0.17	0.0	0	0.39	0.0	0	0.20	0.0	0	0.15	0.0	0	0.91	0.0
Ovary, fallopian tubes	0	0.77	0.0	0	1.96	0.0	1	1.06	0.9	1	0.97	1.0	2	4.77	0.4
Kidney, renal pelvis, ureter	1	0.28	3.6	0	0.71	0.0	0	0.38	0.0	1	0.36	2.8	2	1.73	1.2
Bladder, other urinary	0	0.50	0.0	0	1.28	0.0	1	0.69	1.5	4	0.67	6.0[b]	5	3.13	1.6
Melanoma of the skin	0	0.21	0.0	1	0.56	1.8	0	0.31	0.0	0	0.30	0.0	1	1.38	0.7
Eye	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.18	0.0
Brain, central nervous system	0	0.18	0.0	1	0.47	2.1	1	0.25	3.9	0	0.23	0.0	2	1.15	1.7
Thyroid gland	0	0.13	0.0	1	0.33	3.1	0	0.18	0.0	1	0.17	5.9	2	0.80	2.5
Bone	0	0.03	0.0	0	0.06	0.0	1	0.03	31.3	0	0.03	0.0	1	0.15	6.9
Connective tissue	0	0.07	0.0	2	0.19	10.7[b]	0	0.10	0.0	0	0.09	0.0	2	0.45	4.4
Lymphatic, hematopoietic system	**2**	**1.18**	**1.7**	**1**	**2.98**	**0.3**	**1**	**1.60**	**0.6**	**2**	**1.55**	**1.3**	**6**	**7.31**	**0.8**
Non-Hodgkin's lymphoma	0	0.45	0.0	1	1.15	0.9	0	0.62	0.0	2	0.59	3.4	3	2.81	1.1
Hodgkin's disease	0	0.08	0.0	0	0.21	0.0	1	0.11	9.1	0	0.10	0.0	1	0.50	2.0
Multiple myeloma	1	0.21	4.8	0	0.53	0.0	0	0.28	0.0	0	0.28	0.0	1	1.31	0.8
Leukemias	1	0.43	2.3	0	1.08	0.0	0	0.59	0.0	0	0.57	0.0	1	2.67	0.4
Chronic lymphocytic	0	0.12	0.0	0	0.31	0.0	0	0.17	0.0	0	0.17	0.0	0	0.78	0.0
Acute nonlymphocytic	1	0.15	6.7	0	0.38	0.0	0	0.21	0.0	0	0.21	0.0	1	0.94	1.1

[a] ICD-O morphology codes = 9590–9642, 9690–9701, 9750.

[b] $P < .05$.

HODGKIN'S DISEASE
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial Hodgkin's disease, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,821	1,390	3,211
No. who developed a second primary cancer	56	41	97
Average age at diagnosis of first cancer, yr	40	40	40
Average yr of diagnosis of first cancer	1965	1965	1965
Person-yr of follow-up	8,446	7,753	16,199
Average follow-up, yr	4.6	5.6	5.0
Percent given radiotherapy for first cancer	64.1	67.6	65.6

[a] ICD-O morphology codes = 9650–9662.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial Hodgkin's disease in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	91	93.8
Only the first cancer	3	3.1
Only the second cancer	3	3.1
Neither first nor second cancer	0	0.0
Total second primary cancers	97	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

HODGKIN'S DISEASE
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial Hodgkin's disease among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,211			2,482			1,193			516			3,211		
Person-yr in interval	2,293			6,776			4,015			3,115			16,199		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**10**	**7.99**	**1.3**	**27**	**20.09**	**1.3**	**28**	**12.70**	**2.2**[b]	**32**	**16.34**	**2.0**[b]	**97**	**57.08**	**1.7**[b]
All excluding site of initial cancer	**10**	**7.88**	**1.3**	**27**	**19.78**	**1.4**	**28**	**12.52**	**2.2**[b]	**32**	**16.21**	**2.0**[b]	**97**	**56.35**	**1.7**[b]
Buccal cavity, pharynx	**1**	**0.33**	**3.0**	**2**	**0.83**	**2.4**	**4**	**0.50**	**7.9**[b]	**0**	**0.58**	**0.0**	**7**	**2.24**	**3.1**[b]
Lip	0	0.05	0.0	0	0.12	0.0	1	0.06	16.0	0	0.06	0.0	1	0.29	3.4
Tongue	0	0.06	0.0	0	0.16	0.0	1	0.10	9.7	0	0.12	0.0	1	0.45	2.2
Salivary gland	0	0.02	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.17	0.0
Gum, other mouth	0	0.09	0.0	0	0.24	0.0	1	0.15	6.8	0	0.18	0.0	1	0.66	1.5
Pharynx	1	0.08	12.1	1	0.21	4.7	1	0.13	7.6	0	0.16	0.0	3	0.58	5.1[b]
Digestive system	**3**	**2.31**	**1.3**	**2**	**5.41**	**0.4**	**2**	**3.25**	**0.6**	**6**	**4.17**	**1.4**	**13**	**15.13**	**0.9**
Esophagus	0	0.12	0.0	0	0.30	0.0	0	0.18	0.0	0	0.21	0.0	0	0.81	0.0
Stomach	0	0.39	0.0	0	0.86	0.0	1	0.48	2.1	0	0.54	0.0	1	2.27	0.4
Colon	1	0.91	1.1	1	2.14	0.5	1	1.32	0.8	3	1.79	1.7	6	6.16	1.0
Rectum	0	0.48	0.0	0	1.15	0.0	0	0.68	0.0	2	0.88	2.3	2	3.18	0.6
Liver, biliary	2	0.13	15.3[b]	1	0.30	3.3	0	0.18	0.0	0	0.22	0.0	3	0.83	3.6
Pancreas	0	0.23	0.0	0	0.55	0.0	0	0.33	0.0	1	0.44	2.3	1	1.55	0.6
Respiratory system	**2**	**1.16**	**1.7**	**7**	**2.98**	**2.3**	**3**	**1.87**	**1.6**	**13**	**2.48**	**5.2**[b]	**25**	**8.48**	**2.9**[b]
Nasal cavities, sinuses	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.12	0.0
Larynx	1	0.13	7.5	0	0.34	0.0	0	0.21	0.0	1	0.25	3.9	2	0.94	2.1
Trachea, bronchus, lung	1	0.99	1.0	7	2.56	2.7[b]	3	1.61	1.9	12	2.17	5.5[b]	23	7.33	3.1[b]
Female breast	1	0.92	1.1	3	2.49	1.2	3	1.83	1.6	8	2.65	3.0[b]	15	7.88	1.9[b]
Female genital tract	**0**	**0.61**	**0.0**	**1**	**1.61**	**0.6**	**2**	**1.11**	**1.8**	**2**	**1.49**	**1.3**	**5**	**4.81**	**1.0**
Cervix uteri	0	0.15	0.0	0	0.43	0.0	0	0.30	0.0	0	0.32	0.0	0	1.20	0.0
Corpus uteri	0	0.22	0.0	0	0.58	0.0	2	0.40	5.0	0	0.63	0.0	2	1.83	1.1
Uterus, NOS	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Ovary, fallopian tubes	0	0.17	0.0	1	0.44	2.3	0	0.31	0.0	1	0.42	2.4	2	1.34	1.5
Prostate gland	2	0.65	3.1	1	1.45	0.7	2	0.80	2.5	0	1.14	0.0	5	4.04	1.2
Testis	0	0.05	0.0	0	0.17	0.0	0	0.11	0.0	0	0.06	0.0	0	0.40	0.0
Kidney, renal pelvis, ureter	0	0.18	0.0	1	0.44	2.3	1	0.28	3.6	0	0.35	0.0	2	1.24	1.6
Bladder, other urinary	0	0.39	0.0	3	0.95	3.1	1	0.58	1.7	1	0.77	1.3	5	2.69	1.9
Melanoma of the skin	0	0.14	0.0	1	0.43	2.3	0	0.31	0.0	0	0.33	0.0	1	1.21	0.8
Eye	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.10	0.0
Brain, central nervous system	0	0.13	0.0	0	0.36	0.0	2	0.23	8.7	0	0.24	0.0	2	0.96	2.1
Thyroid gland	0	0.07	0.0	1	0.22	4.5	1	0.16	6.3	2	0.15	13.2[b]	4	0.60	6.7[b]
Bone	0	0.02	0.0	0	0.06	0.0	1	0.03	30.8	0	0.02	0.0	1	0.14	7.1
Connective tissue	0	0.05	0.0	0	0.14	0.0	2	0.08	23.8[b]	0	0.09	0.0	2	0.36	5.5
Lymphatic, hematopoietic system	**1**	**0.62**	**1.6**	**3**	**1.61**	**1.9**	**2**	**0.99**	**2.0**	**0**	**1.12**	**0.0**	**6**	**4.34**	**1.4**
Non-Hodgkin's lymphoma	1	0.20	4.9	1	0.54	1.9	1	0.34	2.9	0	0.42	0.0	3	1.50	2.0
Hodgkin's disease	0	0.11	0.0	0	0.31	0.0	0	0.18	0.0	0	0.13	0.0	0	0.73	0.0
Multiple myeloma	0	0.07	0.0	1	0.19	5.3	0	0.12	0.0	0	0.17	0.0	1	0.55	1.8
Leukemias	0	0.23	0.0	1	0.57	1.7	1	0.35	2.9	0	0.41	0.0	2	1.56	1.3
Chronic lymphocytic	0	0.06	0.0	0	0.14	0.0	0	0.09	0.0	0	0.11	0.0	0	0.40	0.0
Acute nonlymphocytic	0	0.07	0.0	1	0.20	5.0	1	0.13	7.9	0	0.15	0.0	2	0.55	3.7

[a] ICD-O morphology codes = 9650–9662.

[b] $P < .05$.

HODGKIN'S DISEASE
MALES

TABLE 2D. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial Hodgkin's disease among males in Connecticut, 1935-82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	1,821			1,388			638			245			1,821		
Person-yr in interval	1,290			3,694			2,078			1,384			8,446		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**9**	**4.65**	**1.9**	**17**	**11.41**	**1.5**	**19**	**6.63**	**2.9**[b]	**11**	**7.88**	**1.4**	**56**	**30.55**	**1.8**[b]
All excluding site of initial cancer	**9**	**4.58**	**2.0**	**17**	**11.21**	**1.5**	**19**	**6.52**	**2.9**[b]	**11**	**7.80**	**1.4**	**56**	**30.10**	**1.9**[b]
Buccal cavity, pharynx	**1**	**0.27**	**3.7**	**2**	**0.67**	**3.0**	**4**	**0.39**	**10.1**[b]	**0**	**0.42**	**0.0**	**7**	**1.76**	**4.0**[b]
Lip	0	0.05	0.0	0	0.11	0.0	1	0.06	17.3	0	0.05	0.0	1	0.27	3.7
Tongue	0	0.05	0.0	0	0.13	0.0	1	0.08	12.4	0	0.08	0.0	1	0.35	2.9
Salivary gland	0	0.01	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Gum, other mouth	0	0.08	0.0	0	0.19	0.0	1	0.11	9.0	0	0.12	0.0	1	0.50	2.0
Pharynx	1	0.07	14.4	1	0.18	5.6	1	0.11	9.4	0	0.12	0.0	3	0.47	6.4[b]
Digestive system	**3**	**1.43**	**2.1**	**0**	**3.35**	**0.0**	**2**	**1.88**	**1.1**	**2**	**2.25**	**0.9**	**7**	**8.91**	**0.8**
Esophagus	0	0.10	0.0	0	0.25	0.0	0	0.14	0.0	0	0.16	0.0	0	0.65	0.0
Stomach	0	0.28	0.0	0	0.62	0.0	1	0.32	3.1	0	0.34	0.0	1	1.55	0.6
Colon	1	0.50	2.0	0	1.17	0.0	1	0.67	1.5	2	0.87	2.3	4	3.21	1.2
Rectum	0	0.31	0.0	0	0.73	0.0	0	0.41	0.0	0	0.49	0.0	0	1.93	0.0
Liver, biliary	2	0.07	27.7[b]	0	0.17	0.0	0	0.10	0.0	0	0.11	0.0	2	0.45	4.4
Pancreas	0	0.14	0.0	0	0.34	0.0	0	0.20	0.0	0	0.24	0.0	0	0.93	0.0
Respiratory system	**2**	**0.96**	**2.1**	**5**	**2.44**	**2.1**	**3**	**1.48**	**2.0**	**8**	**1.84**	**4.4**[b]	**18**	**6.71**	**2.7**[b]
Nasal cavities, sinuses	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Larynx	1	0.12	8.3	0	0.31	0.0	0	0.19	0.0	1	0.21	4.7	2	0.83	2.4
Trachea, bronchus, lung	1	0.82	1.2	5	2.08	2.4	3	1.26	2.4	7	1.59	4.4[b]	16	5.74	2.8[b]
Prostate gland	2	0.65	3.1	1	1.45	0.7	2	0.80	2.5	0	1.14	0.0	5	4.04	1.2
Testis	0	0.05	0.0	0	0.17	0.0	0	0.11	0.0	0	0.06	0.0	0	0.40	0.0
Kidney, renal pelvis, ureter	0	0.13	0.0	1	0.32	3.1	1	0.19	5.2	0	0.22	0.0	2	0.86	2.3
Bladder, other urinary	0	0.31	0.0	3	0.76	4.0	1	0.44	2.3	1	0.57	1.8	5	2.08	2.4
Melanoma of the skin	0	0.08	0.0	0	0.25	0.0	0	0.16	0.0	0	0.16	0.0	0	0.65	0.0
Eye	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Brain, central nervous system	0	0.08	0.0	0	0.23	0.0	2	0.14	14.1[b]	0	0.13	0.0	2	0.59	3.4
Thyroid gland	0	0.02	0.0	0	0.07	0.0	0	0.05	0.0	0	0.04	0.0	0	0.18	0.0
Bone	0	0.01	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.09	0.0
Connective tissue	0	0.03	0.0	0	0.09	0.0	1	0.05	19.8	0	0.05	0.0	1	0.22	4.5
Lymphatic, hematopoietic system	**1**	**0.38**	**2.6**	**3**	**0.99**	**3.0**	**1**	**0.58**	**1.7**	**0**	**0.60**	**0.0**	**5**	**2.56**	**2.0**
Non-Hodgkin's lymphoma	1	0.12	8.2	1	0.32	3.1	1	0.20	5.1	0	0.21	0.0	3	0.85	3.5
Hodgkin's disease	0	0.07	0.0	0	0.20	0.0	0	0.11	0.0	0	0.08	0.0	0	0.45	0.0
Multiple myeloma	0	0.04	0.0	1	0.11	9.4	0	0.06	0.0	0	0.08	0.0	1	0.30	3.4
Leukemias	0	0.15	0.0	1	0.37	2.7	0	0.21	0.0	0	0.23	0.0	1	0.96	1.0
Chronic lymphocytic	0	0.04	0.0	0	0.10	0.0	0	0.06	0.0	0	0.07	0.0	0	0.26	0.0
Acute nonlymphocytic	0	0.05	0.0	1	0.12	8.5	0	0.07	0.0	0	0.08	0.0	1	0.31	3.2

[a] ICD-O morphology codes = 9650-9662.
[b] $P < .05$.

HODGKIN'S DISEASE FEMALES

TABLE 2E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial Hodgkin's disease among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,390			1,094			555			271			1,390		
Person-yr in interval	1,003			3,082			1,937			1,731			7,753		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1**	**3.34**	**0.3**	**10**	**8.68**	**1.2**	**9**	**6.06**	**1.5**	**21**	**8.46**	**2.5**[b]	**41**	**26.52**	**1.5**[b]
All excluding site of initial cancer	**1**	**3.30**	**0.3**	**10**	**8.56**	**1.2**	**9**	**5.99**	**1.5**	**21**	**8.40**	**2.5**[b]	**41**	**26.23**	**1.6**[b]
Buccal cavity, pharynx	**0**	**0.06**	**0.0**	**0**	**0.15**	**0.0**	**0**	**0.11**	**0.0**	**0**	**0.16**	**0.0**	**0**	**0.49**	**0.0**
Lip	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0
Tongue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.10	0.0
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Gum, other mouth	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.06	0.0	0	0.16	0.0
Pharynx	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.11	0.0
Digestive system	**0**	**0.88**	**0.0**	**2**	**2.06**	**1.0**	**0**	**1.37**	**0.0**	**4**	**1.91**	**2.1**	**6**	**6.22**	**1.0**
Esophagus	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.05	0.0	0	0.16	0.0
Stomach	0	0.11	0.0	0	0.24	0.0	0	0.16	0.0	0	0.20	0.0	0	0.71	0.0
Colon	0	0.41	0.0	1	0.97	1.0	0	0.65	0.0	1	0.92	1.1	2	2.95	0.7
Rectum	0	0.17	0.0	0	0.41	0.0	0	0.27	0.0	2	0.39	5.1	2	1.25	1.6
Liver, biliary	0	0.06	0.0	1	0.13	7.7	0	0.08	0.0	0	0.11	0.0	1	0.38	2.6
Pancreas	0	0.09	0.0	0	0.20	0.0	0	0.13	0.0	1	0.20	5.0	1	0.62	1.6
Respiratory system	**0**	**0.20**	**0.0**	**2**	**0.54**	**3.7**	**0**	**0.39**	**0.0**	**5**	**0.64**	**7.8**[b]	**7**	**1.78**	**3.9**[b]
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.04	0.0	0	0.11	0.0
Trachea, bronchus, lung	0	0.18	0.0	2	0.49	4.1	0	0.35	0.0	5	0.58	8.6[b]	7	1.60	4.4[b]
Female breast	1	0.92	1.1	3	2.49	1.2	3	1.83	1.6	8	2.65	3.0[b]	15	7.88	1.9[b]
Female genital tract	**0**	**0.61**	**0.0**	**1**	**1.61**	**0.6**	**2**	**1.11**	**1.8**	**2**	**1.49**	**1.3**	**5**	**4.81**	**1.0**
Cervix uteri	0	0.15	0.0	0	0.43	0.0	0	0.30	0.0	0	0.32	0.0	0	1.20	0.0
Corpus uteri	0	0.22	0.0	0	0.58	0.0	2	0.40	5.0	0	0.63	0.0	2	1.83	1.1
Uterus, NOS	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Ovary, fallopian tubes	0	0.17	0.0	1	0.44	2.3	0	0.31	0.0	1	0.42	2.4	2	1.34	1.5
Kidney, renal pelvis, ureter	0	0.05	0.0	0	0.12	0.0	0	0.08	0.0	0	0.12	0.0	0	0.38	0.0
Bladder, other urinary	0	0.08	0.0	0	0.20	0.0	0	0.13	0.0	0	0.20	0.0	0	0.61	0.0
Melanoma of the skin	0	0.06	0.0	1	0.19	5.4	0	0.15	0.0	0	0.18	0.0	1	0.56	1.8
Eye	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Brain, central nervous system	0	0.05	0.0	0	0.13	0.0	0	0.09	0.0	0	0.11	0.0	0	0.37	0.0
Thyroid gland	0	0.04	0.0	1	0.15	6.7	1	0.11	8.9	2	0.11	17.9[b]	4	0.42	9.6[b]
Bone	0	0.01	0.0	0	0.02	0.0	1	0.01	84.1[b]	0	0.01	0.0	1	0.05	19.0
Connective tissue	0	0.02	0.0	0	0.05	0.0	1	0.03	29.7	0	0.04	0.0	1	0.14	7.0
Lymphatic, hematopoietic system	**0**	**0.23**	**0.0**	**0**	**0.62**	**0.0**	**1**	**0.41**	**2.5**	**0**	**0.52**	**0.0**	**1**	**1.78**	**0.6**
Non-Hodgkin's lymphoma	0	0.08	0.0	0	0.21	0.0	0	0.15	0.0	0	0.21	0.0	0	0.65	0.0
Hodgkin's disease	0	0.04	0.0	0	0.12	0.0	0	0.07	0.0	0	0.06	0.0	0	0.29	0.0
Multiple myeloma	0	0.03	0.0	0	0.08	0.0	0	0.05	0.0	0	0.08	0.0	0	0.25	0.0
Leukemias	0	0.08	0.0	0	0.21	0.0	1	0.14	7.4	0	0.17	0.0	1	0.60	1.7
Chronic lymphocytic	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.04	0.0	0	0.14	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.08	0.0	1	0.06	18.0	0	0.07	0.0	1	0.24	4.3

[a] ICD-O morphology codes = 9650–9662.

[b] $P < .05$.

MULTIPLE MYELOMA
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial multiple myeloma, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,107	1,142	2,249
No. who developed a second primary cancer	46	27	73
Average age at diagnosis of first cancer, yr	64	67	65
Average yr of diagnosis of first cancer	1968	1969	1969
Person-yr of follow-up	2,258	2,247	4,505
Average follow-up, yr	2.0	2.0	2.0
Percent given radiotherapy for first cancer	39.7	36.6	38.1

[a] ICD-O morphology codes = 9730–9731.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial multiple myeloma in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	56	76.7
Only the first cancer	3	4.1
Only the second cancer	13	17.8
Neither first nor second cancer	1	1.4
Total second primary cancers	73	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

MULTIPLE MYELOMA
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial multiple myeloma among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	2,249			1,335			225			43			2,249		
Person-yr in interval	1,374			2,414			537			181			4,505		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**19**	**17.36**	**1.1**	**40**	**31.48**	**1.3**	**9**	**7.12**	**1.3**	**5**	**3.03**	**1.7**	**73**	**58.94**	**1.2**
All excluding site of initial cancer	**19**	**17.15**	**1.1**	**40**	**31.10**	**1.3**	**9**	**7.03**	**1.3**	**5**	**2.99**	**1.7**	**73**	**58.22**	**1.3**
Buccal cavity, pharynx	**0**	**0.60**	**0.0**	**0**	**1.06**	**0.0**	**1**	**0.25**	**4.0**	**0**	**0.10**	**0.0**	**1**	**2.00**	**0.5**
Lip	0	0.08	0.0	0	0.13	0.0	0	0.03	0.0	0	0.02	0.0	0	0.26	0.0
Tongue	0	0.12	0.0	0	0.21	0.0	0	0.05	0.0	0	0.02	0.0	0	0.40	0.0
Salivary gland	0	0.04	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.14	0.0
Gum, other mouth	0	0.18	0.0	0	0.33	0.0	1	0.08	13.1	0	0.03	0.0	1	0.61	1.6
Pharynx	0	0.15	0.0	0	0.27	0.0	0	0.07	0.0	0	0.02	0.0	0	0.51	0.0
Digestive system	**6**	**5.38**	**1.1**	**16**	**9.64**	**1.7**	**0**	**2.17**	**0.0**	**1**	**0.95**	**1.1**	**23**	**18.13**	**1.3**
Esophagus	0	0.25	0.0	1	0.44	2.3	0	0.10	0.0	1	0.04	23.6	2	0.83	2.4
Stomach	2	0.76	2.6	3	1.27	2.4	0	0.28	0.0	0	0.13	0.0	5	2.44	2.0
Colon	3	2.33	1.3	6	4.26	1.4	0	0.95	0.0	0	0.43	0.0	9	7.96	1.1
Rectum	0	1.09	0.0	2	1.95	1.0	0	0.44	0.0	0	0.18	0.0	2	3.65	0.5
Liver, biliary	1	0.31	3.3	0	0.55	0.0	0	0.12	0.0	0	0.05	0.0	1	1.03	1.0
Pancreas	0	0.56	0.0	3	1.02	3.0	0	0.23	0.0	0	0.10	0.0	3	1.90	1.6
Respiratory system	**1**	**2.60**	**0.4**	**7**	**4.89**	**1.4**	**2**	**1.17**	**1.7**	**0**	**0.47**	**0.0**	**10**	**9.11**	**1.1**
Nasal cavities, sinuses	0	0.03	0.0	0	0.06	0.0	0	0.01	0.0	0	0.01	0.0	0	0.11	0.0
Larynx	0	0.25	0.0	0	0.46	0.0	0	0.11	0.0	0	0.04	0.0	0	0.86	0.0
Trachea, bronchus, lung	1	2.29	0.4	7	4.33	1.6	2	1.03	1.9	0	0.42	0.0	10	8.06	1.2
Female breast	3	1.88	1.6	0	3.46	0.0	1	0.76	1.3	0	0.21	0.0	4	6.30	0.6
Female genital tract	**1**	**1.13**	**0.9**	**1**	**1.99**	**0.5**	**1**	**0.42**	**2.4**	**0**	**0.10**	**0.0**	**3**	**3.64**	**0.8**
Cervix uteri	1	0.19	5.4	0	0.29	0.0	1	0.06	17.7	0	0.01	0.0	2	0.55	3.6
Corpus uteri	0	0.50	0.0	0	0.92	0.0	0	0.21	0.0	0	0.05	0.0	0	1.68	0.0
Uterus, NOS	0	0.06	0.0	0	0.08	0.0	0	0.01	0.0	0	0.00	0.0	0	0.16	0.0
Ovary, fallopian tubes	0	0.31	0.0	1	0.56	1.8	0	0.12	0.0	0	0.03	0.0	1	1.02	1.0
Prostate gland	3	1.84	1.6	2	3.26	0.6	2	0.72	2.8	2	0.48	4.2	9	6.28	1.4
Testis	0	0.01	0.0	0	0.03	0.0	0	0.01	0.0	0	0.00	0.0	0	0.05	0.0
Kidney, renal pelvis, ureter	2	0.37	5.4	1	0.68	1.5	0	0.16	0.0	0	0.06	0.0	3	1.27	2.4
Bladder, other urinary	1	0.96	1.0	1	1.76	0.6	0	0.40	0.0	0	0.20	0.0	2	3.31	0.6
Melanoma of the skin	0	0.20	0.0	1	0.38	2.6	0	0.09	0.0	0	0.03	0.0	1	0.69	1.4
Eye	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.00	0.0	0	0.08	0.0
Brain, central nervous system	0	0.18	0.0	0	0.33	0.0	0	0.08	0.0	0	0.03	0.0	0	0.62	0.0
Thyroid gland	1	0.07	13.7	0	0.13	0.0	0	0.03	0.0	0	0.01	0.0	1	0.24	4.2
Bone	0	0.02	0.0	0	0.04	0.0	0	0.01	0.0	0	0.00	0.0	0	0.07	0.0
Connective tissue	0	0.08	0.0	0	0.14	0.0	0	0.03	0.0	0	0.01	0.0	0	0.26	0.0
Lymphatic, hematopoietic system	**0**	**1.19**	**0.0**	**10**	**2.17**	**4.6**[b]	**2**	**0.49**	**4.1**	**0**	**0.21**	**0.0**	**12**	**4.07**	**3.0**[b]
Non-Hodgkin's lymphoma	0	0.41	0.0	2	0.77	2.6	0	0.18	0.0	0	0.07	0.0	2	1.44	1.4
Hodgkin's disease	0	0.07	0.0	0	0.13	0.0	0	0.03	0.0	0	0.01	0.0	0	0.24	0.0
Multiple myeloma	0	0.21	0.0	0	0.38	0.0	0	0.09	0.0	0	0.04	0.0	0	0.72	0.0
Leukemias	0	0.49	0.0	8	0.88	9.1[b]	2	0.20	10.1[b]	0	0.09	0.0	10	1.67	6.0[b]
Chronic lymphocytic	0	0.16	0.0	0	0.29	0.0	0	0.07	0.0	0	0.03	0.0	0	0.54	0.0
Acute nonlymphocytic	0	0.16	0.0	7	0.30	23.2[b]	2	0.07	30.3[b]	0	0.03	0.0	9	0.56	16.0[b]

[a] ICD-O morphology codes = 9730–9731.

[b] $P < .05$.

MULTIPLE MYELOMA
MALES

TABLE 3D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial multiple myeloma among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,107			653			115			27			1,107		
Person-yr in interval	668			1,189			281			120			2,258		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**12**	**9.87**	**1.2**	**25**	**17.59**	**1.4**	**4**	**4.06**	**1.0**	**5**	**2.14**	**2.3**	**46**	**33.63**	**1.4**^{b}
All excluding site of initial cancer	**12**	**9.76**	**1.2**	**25**	**17.40**	**1.4**	**4**	**4.02**	**1.0**	**5**	**2.12**	**2.4**	**46**	**33.27**	**1.4**^{b}
Buccal cavity, pharynx	**0**	**0.47**	**0.0**	**0**	**0.81**	**0.0**	**1**	**0.19**	**5.2**	**0**	**0.08**	**0.0**	**1**	**1.55**	**0.6**
Lip	0	0.08	0.0	0	0.12	0.0	0	0.03	0.0	0	0.02	0.0	0	0.24	0.0
Tongue	0	0.09	0.0	0	0.16	0.0	0	0.04	0.0	0	0.01	0.0	0	0.31	0.0
Salivary gland	0	0.02	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Gum, other mouth	0	0.13	0.0	0	0.24	0.0	1	0.06	18.0	0	0.02	0.0	1	0.45	2.2
Pharynx	0	0.12	0.0	0	0.22	0.0	0	0.05	0.0	0	0.02	0.0	0	0.41	0.0
Digestive system	**4**	**3.03**	**1.3**	**8**	**5.29**	**1.5**	**0**	**1.23**	**0.0**	**1**	**0.64**	**1.6**	**13**	**10.17**	**1.3**
Esophagus	0	0.20	0.0	1	0.34	3.0	0	0.08	0.0	1	0.04	28.1	2	0.65	3.1
Stomach	2	0.49	4.0	2	0.81	2.5	0	0.19	0.0	0	0.10	0.0	4	1.59	2.5
Colon	2	1.19	1.7	2	2.11	0.9	0	0.48	0.0	0	0.27	0.0	4	4.05	1.0
Rectum	0	0.64	0.0	0	1.12	0.0	0	0.26	0.0	0	0.12	0.0	0	2.13	0.0
Liver, biliary	0	0.16	0.0	0	0.28	0.0	0	0.06	0.0	0	0.03	0.0	0	0.53	0.0
Pancreas	0	0.31	0.0	2	0.55	3.6	0	0.13	0.0	0	0.07	0.0	2	1.05	1.9
Respiratory system	**1**	**2.09**	**0.5**	**6**	**3.85**	**1.6**	**1**	**0.91**	**1.1**	**0**	**0.41**	**0.0**	**8**	**7.25**	**1.1**
Nasal cavities, sinuses	0	0.02	0.0	0	0.04	0.0	0	0.01	0.0	0	0.00	0.0	0	0.07	0.0
Larynx	0	0.22	0.0	0	0.40	0.0	0	0.10	0.0	0	0.03	0.0	0	0.76	0.0
Trachea, bronchus, lung	1	1.83	0.5	6	3.38	1.8	1	0.80	1.3	0	0.37	0.0	8	6.36	1.3
Prostate gland	3	1.84	1.6	2	3.26	0.6	2	0.72	2.8	2	0.48	4.2	9	6.28	1.4
Testis	0	0.01	0.0	0	0.03	0.0	0	0.01	0.0	0	0.00	0.0	0	0.05	0.0
Kidney, renal pelvis, ureter	1	0.25	4.0	1	0.45	2.2	0	0.11	0.0	0	0.05	0.0	2	0.86	2.3
Bladder, other urinary	1	0.73	1.4	1	1.33	0.8	0	0.30	0.0	0	0.17	0.0	2	2.53	0.8
Melanoma of the skin	0	0.11	0.0	1	0.22	4.5	0	0.05	0.0	0	0.02	0.0	1	0.41	2.5
Eye	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.04	0.0
Brain, central nervous system	0	0.11	0.0	0	0.20	0.0	0	0.05	0.0	0	0.02	0.0	0	0.37	0.0
Thyroid gland	1	0.03	38.9	0	0.05	0.0	0	0.01	0.0	0	0.00	0.0	1	0.09	11.4
Bone	0	0.01	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.04	0.0
Connective tissue	0	0.05	0.0	0	0.08	0.0	0	0.02	0.0	0	0.01	0.0	0	0.16	0.0
Lymphatic, hematopoietic system	**0**	**0.67**	**0.0**	**5**	**1.18**	**4.2**^{b}	**0**	**0.27**	**0.0**	**0**	**0.14**	**0.0**	**5**	**2.26**	**2.2**
Non-Hodgkin's lymphoma	0	0.22	0.0	0	0.39	0.0	0	0.09	0.0	0	0.05	0.0	0	0.75	0.0
Hodgkin's disease	0	0.04	0.0	0	0.08	0.0	0	0.02	0.0	0	0.01	0.0	0	0.14	0.0
Multiple myeloma	0	0.11	0.0	0	0.19	0.0	0	0.04	0.0	0	0.02	0.0	0	0.36	0.0
Leukemias	0	0.30	0.0	5	0.52	9.6^b	0	0.12	0.0	0	0.07	0.0	5	1.00	5.0^b
Chronic lymphocytic	0	0.10	0.0	0	0.18	0.0	0	0.04	0.0	0	0.02	0.0	0	0.34	0.0
Acute nonlymphocytic	0	0.09	0.0	4	0.17	23.6^b	0	0.04	0.0	0	0.02	0.0	4	0.32	12.5^b

[a] ICD-O morphology codes = 9730–9731.

[b] $P < .05$.

MULTIPLE MYELOMA
FEMALES

TABLE 3E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial multiple myeloma among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,142			682			110			16			1,142		
Person-yr in interval	706			1,224			256			61			2,247		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**7**	**7.49**	**0.9**	**15**	**13.89**	**1.1**	**5**	**3.06**	**1.6**	**0**	**0.89**	**0.0**	**27**	**25.31**	**1.1**
All excluding site of initial cancer	**7**	**7.39**	**0.9**	**15**	**13.70**	**1.1**	**5**	**3.02**	**1.7**	**0**	**0.88**	**0.0**	**27**	**24.96**	**1.1**
Buccal cavity, pharynx	**0**	**0.13**	**0.0**	**0**	**0.25**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.01**	**0.0**	**0**	**0.45**	**0.0**
Lip	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Tongue	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.00	0.0	0	0.09	0.0
Salivary gland	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.00	0.0	0	0.05	0.0
Gum, other mouth	0	0.05	0.0	0	0.09	0.0	0	0.02	0.0	0	0.01	0.0	0	0.16	0.0
Pharynx	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.00	0.0	0	0.10	0.0
Digestive system	**2**	**2.35**	**0.9**	**8**	**4.35**	**1.8**	**0**	**0.95**	**0.0**	**0**	**0.31**	**0.0**	**10**	**7.95**	**1.3**
Esophagus	0	0.05	0.0	0	0.10	0.0	0	0.02	0.0	0	0.01	0.0	0	0.18	0.0
Stomach	0	0.27	0.0	1	0.46	2.2	0	0.09	0.0	0	0.03	0.0	1	0.85	1.2
Colon	1	1.14	0.9	4	2.15	1.9	0	0.47	0.0	0	0.16	0.0	5	3.92	1.3
Rectum	0	0.45	0.0	2	0.83	2.4	0	0.18	0.0	0	0.06	0.0	2	1.52	1.3
Liver, biliary	1	0.15	6.6	0	0.27	0.0	0	0.06	0.0	0	0.02	0.0	1	0.50	2.0
Pancreas	0	0.25	0.0	1	0.47	2.1	0	0.10	0.0	0	0.03	0.0	1	0.85	1.2
Respiratory system	**0**	**0.51**	**0.0**	**1**	**1.04**	**1.0**	**1**	**0.25**	**4.0**	**0**	**0.06**	**0.0**	**2**	**1.86**	**1.1**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.04	0.0
Larynx	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.00	0.0	0	0.10	0.0
Trachea, bronchus, lung	0	0.47	0.0	1	0.95	1.1	1	0.23	4.3	0	0.05	0.0	2	1.70	1.2
Female breast	3	1.88	1.6	0	3.46	0.0	1	0.76	1.3	0	0.21	0.0	4	6.30	0.6
Female genital tract	**1**	**1.13**	**0.9**	**1**	**1.99**	**0.5**	**1**	**0.42**	**2.4**	**0**	**0.10**	**0.0**	**3**	**3.64**	**0.8**
Cervix uteri	1	0.19	5.4	0	0.29	0.0	1	0.06	17.7	0	0.01	0.0	2	0.55	3.6
Corpus uteri	0	0.50	0.0	0	0.92	0.0	0	0.21	0.0	0	0.05	0.0	0	1.68	0.0
Uterus, NOS	0	0.06	0.0	0	0.08	0.0	0	0.01	0.0	0	0.00	0.0	0	0.16	0.0
Ovary, fallopian tubes	0	0.31	0.0	1	0.56	1.8	0	0.12	0.0	0	0.03	0.0	1	1.02	1.0
Kidney, renal pelvis, ureter	1	0.12	8.2	0	0.23	0.0	0	0.05	0.0	0	0.01	0.0	1	0.41	2.4
Bladder, other urinary	0	0.22	0.0	0	0.43	0.0	0	0.10	0.0	0	0.03	0.0	0	0.78	0.0
Melanoma of the skin	0	0.08	0.0	0	0.16	0.0	0	0.04	0.0	0	0.01	0.0	0	0.29	0.0
Eye	0	0.01	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.04	0.0
Brain, central nervous system	0	0.07	0.0	0	0.14	0.0	0	0.03	0.0	0	0.01	0.0	0	0.25	0.0
Thyroid gland	0	0.05	0.0	0	0.08	0.0	0	0.02	0.0	0	0.00	0.0	0	0.15	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Connective tissue	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.00	0.0	0	0.10	0.0
Lymphatic, hematopoietic system	**0**	**0.52**	**0.0**	**5**	**0.99**	**5.0**^{b}	**2**	**0.22**	**9.0**^{b}	**0**	**0.07**	**0.0**	**7**	**1.81**	**3.9**^{b}
Non-Hodgkin's lymphoma	0	0.20	0.0	2	0.38	5.2	0	0.09	0.0	0	0.03	0.0	2	0.69	2.9
Hodgkin's disease	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.00	0.0	0	0.10	0.0
Multiple myeloma	0	0.10	0.0	0	0.19	0.0	0	0.04	0.0	0	0.01	0.0	0	0.35	0.0
Leukemias	0	0.19	0.0	3	0.36	8.3^b	2	0.08	25.0^b	0	0.03	0.0	5	0.66	7.5^b
Chronic lymphocytic	0	0.06	0.0	0	0.11	0.0	0	0.02	0.0	0	0.01	0.0	0	0.20	0.0
Acute nonlymphocytic	0	0.07	0.0	3	0.13	22.7^b	2	0.03	66.8^b	0	0.01	0.0	5	0.24	20.8^b

[a] ICD-O morphology codes = 9730–9731.

[b] $P < .05$.

LEUKEMIA
BOTH SEXES

TABLE 4A.—*Characteristics of persons reported to the Connecticut Tumor Registry with an initial leukemia, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	3,878	2,849	6,727
No. who developed a second primary cancer	184	80	264
Average age at diagnosis of first cancer, yr	53	54	53
Average yr of diagnosis of first cancer	1966	1966	1966
Person-yr of follow-up	9,866	7,680	17,546
Average follow-up, yr	2.5	2.7	2.6
Percent given radiotherapy for first cancer	19.4	17.7	18.7

[a] ICD-O morphology codes = 9800–9940.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B.—*Microscopic confirmation among persons who developed second primary cancers after an initial leukemia in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	226	85.6
Only the first cancer	21	8.0
Only the second cancer	13	4.9
Neither first nor second cancer	4	1.5
Total second primary cancers	264	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LEUKEMIA
BOTH SEXES

TABLE 4C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial leukemia among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,727			4,045			1,199			318			6,727		
Person-yr in interval	4,105			8,790			3,230			1,422			17,546		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**53**	**40.21**	**1.3**	**128**	**95.83**	**1.3**[b]	**63**	**40.12**	**1.6**[b]	**20**	**21.77**	**0.9**	**264**	**197.77**	**1.3**[b]
All excluding site of initial cancer	**53**	**38.99**	**1.4**[b]	**128**	**92.98**	**1.4**[b]	**63**	**38.94**	**1.6**[b]	**20**	**21.11**	**0.9**	**264**	**191.85**	**1.4**[b]
Buccal cavity, pharynx	**2**	**1.53**	**1.3**	**7**	**3.54**	**2.0**	**1**	**1.41**	**0.7**	**1**	**0.75**	**1.3**	**11**	**7.23**	**1.5**
Lip	2	0.26	7.8	0	0.57	0.0	0	0.22	0.0	0	0.12	0.0	2	1.16	1.7
Tongue	0	0.31	0.0	3	0.70	4.3	0	0.28	0.0	1	0.15	6.8	4	1.43	2.8
Salivary gland	0	0.10	0.0	1	0.24	4.2	0	0.10	0.0	0	0.05	0.0	1	0.48	2.1
Gum, other mouth	0	0.44	0.0	2	1.04	1.9	1	0.42	2.4	0	0.22	0.0	3	2.11	1.4
Pharynx	0	0.37	0.0	1	0.86	1.2	0	0.35	0.0	0	0.18	0.0	1	1.76	0.6
Digestive system	**16**	**12.93**	**1.2**	**42**	**30.64**	**1.4**	**24**	**12.73**	**1.9**[b]	**8**	**6.89**	**1.2**	**90**	**63.13**	**1.4**[b]
Esophagus	0	0.65	0.0	1	1.49	0.7	1	0.60	1.7	1	0.32	3.1	3	3.06	1.0
Stomach	3	2.12	1.4	6	4.83	1.2	2	1.90	1.1	1	1.02	1.0	12	9.87	1.2
Colon	4	5.31	0.8	20	12.83	1.6	9	5.45	1.7	4	2.98	1.3	37	26.55	1.4
Rectum	2	2.57	0.8	8	6.08	1.3	5	2.53	2.0	2	1.35	1.5	17	12.52	1.4
Liver, biliary	2	0.74	2.7	1	1.75	0.6	1	0.73	1.4	0	0.38	0.0	4	3.59	1.1
Pancreas	3	1.31	2.3	2	3.12	0.6	5	1.31	3.8[b]	0	0.72	0.0	10	6.45	1.5
Respiratory system	**11**	**6.00**	**1.8**	**26**	**14.35**	**1.8**[b]	**15**	**6.12**	**2.4**[b]	**5**	**3.43**	**1.5**	**57**	**29.89**	**1.9**[b]
Nasal cavities, sinuses	0	0.08	0.0	1	0.19	5.4	0	0.08	0.0	0	0.04	0.0	1	0.38	2.6
Larynx	0	0.62	0.0	0	1.45	0.0	1	0.59	1.7	0	0.31	0.0	1	2.96	0.3
Trachea, bronchus, lung	11	5.24	2.1[b]	24	12.59	1.9[b]	14	5.41	2.6[b]	5	3.05	1.6	54	26.27	2.1[b]
Female breast	2	3.38	0.6	8	8.41	1.0	1	3.63	0.3	0	1.59	0.0	11	17.00	0.6
Female genital tract	**0**	**2.06**	**0.0**	**2**	**5.02**	**0.4**	**1**	**2.09**	**0.5**	**0**	**0.90**	**0.0**	**3**	**10.05**	**0.3**[b]
Cervix uteri	0	0.39	0.0	0	0.89	0.0	0	0.33	0.0	0	0.13	0.0	0	1.74	0.0
Corpus uteri	0	0.82	0.0	1	2.07	0.5	0	0.92	0.0	0	0.41	0.0	1	4.21	0.2
Uterus, NOS	0	0.15	0.0	0	0.33	0.0	0	0.11	0.0	0	0.04	0.0	0	0.63	0.0
Ovary, fallopian tubes	0	0.56	0.0	0	1.39	0.0	1	0.58	1.7	0	0.26	0.0	1	2.79	0.4
Prostate gland	11	4.99	2.2[b]	26	11.73	2.2[b]	4	4.91	0.8	0	3.16	0.0	41	24.77	1.7[b]
Testis	0	0.05	0.0	1	0.11	9.4	0	0.04	0.0	1	0.02	56.3	2	0.21	9.4[b]
Kidney, renal pelvis, ureter	7	0.87	8.0[b]	3	2.06	1.5	3	0.86	3.5	0	0.46	0.0	13	4.26	3.1[b]
Bladder, other urinary	1	2.34	0.4	4	5.59	0.7	4	2.36	1.7	0	1.38	0.0	9	11.66	0.8
Melanoma of the skin	0	0.43	0.0	3	1.04	2.9	0	0.44	0.0	2	0.22	9.1[b]	5	2.12	2.4
Eye	0	0.06	0.0	0	0.14	0.0	0	0.06	0.0	0	0.03	0.0	0	0.29	0.0
Brain, central nervous system	0	0.40	0.0	2	0.94	2.1	1	0.39	2.6	0	0.19	0.0	3	1.92	1.6
Thyroid gland	0	0.17	0.0	0	0.39	0.0	2	0.16	12.9[b]	0	0.07	0.0	2	0.78	2.6
Bone	0	0.06	0.0	0	0.13	0.0	0	0.05	0.0	0	0.02	0.0	0	0.27	0.0
Connective tissue	0	0.20	0.0	3	0.46	6.6[b]	0	0.18	0.0	0	0.10	0.0	3	0.93	3.2
Lymphatic, hematopoietic system	**1**	**2.75**	**0.4**	**0**	**6.53**	**0.0**[b]	**1**	**2.74**	**0.4**	**2**	**1.50**	**1.3**	**4**	**13.50**	**0.3**[b]
Non-Hodgkin's lymphoma	0	0.90	0.0	0	2.17	0.0	1	0.93	1.1	2	0.49	4.1	3	4.49	0.7
Hodgkin's disease	0	0.19	0.0	0	0.44	0.0	0	0.17	0.0	0	0.09	0.0	0	0.89	0.0
Multiple myeloma	1	0.43	2.3	0	1.06	0.0	0	0.46	0.0	0	0.26	0.0	1	2.21	0.5
Leukemias	0	1.22	0.0	0	2.85	0.0	0	1.18	0.0	0	0.66	0.0	0	5.92	0.0[b]
Chronic lymphocytic	0	0.38	0.0	0	0.90	0.0	0	0.38	0.0	0	0.22	0.0	0	1.87	0.0
Acute nonlymphocytic	0	0.37	0.0	0	0.88	0.0	0	0.38	0.0	0	0.22	0.0	0	1.85	0.0

[a] ICD-O morphology codes = 9800–9940.

[b] $P < .05$.

LEUKEMIA
MALES

TABLE 4D. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial leukemia among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,878			2,331			654			175			3,878		
Person-yr in interval	2,371			4,926			1,728			842			9,866		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**43**	**26.60**	**1.6**[b]	**87**	**61.68**	**1.4**[b]	**41**	**25.31**	**1.6**[b]	**13**	**15.18**	**0.9**	**184**	**128.66**	**1.4**[b]
All excluding site of initial cancer	**43**	**25.76**	**1.7**[b]	**87**	**59.76**	**1.5**[b]	**41**	**24.53**	**1.7**[b]	**13**	**14.70**	**0.9**	**184**	**124.64**	**1.5**[b]
Buccal cavity, pharynx	**2**	**1.31**	**1.5**	**4**	**2.97**	**1.3**	**0**	**1.16**	**0.0**	**1**	**0.64**	**1.6**	**7**	**6.06**	**1.2**
Lip	2	0.24	8.3	0	0.53	0.0	0	0.20	0.0	0	0.11	0.0	2	1.08	1.8
Tongue	0	0.26	0.0	2	0.59	3.4	0	0.23	0.0	1	0.12	8.1	3	1.20	2.5
Salivary gland	0	0.07	0.0	1	0.16	6.2	0	0.06	0.0	0	0.04	0.0	1	0.33	3.0
Gum, other mouth	0	0.36	0.0	1	0.83	1.2	0	0.32	0.0	0	0.18	0.0	1	1.69	0.6
Pharynx	0	0.32	0.0	0	0.75	0.0	0	0.29	0.0	0	0.16	0.0	0	1.52	0.0
Digestive system	**10**	**8.50**	**1.2**	**21**	**19.45**	**1.1**	**15**	**7.88**	**1.9**[b]	**3**	**4.71**	**0.6**	**49**	**40.51**	**1.2**
Esophagus	0	0.56	0.0	1	1.25	0.8	1	0.50	2.0	0	0.28	0.0	2	2.57	0.8
Stomach	2	1.55	1.3	2	3.42	0.6	1	1.32	0.8	1	0.78	1.3	6	7.07	0.8
Colon	2	3.20	0.6	11	7.47	1.5	6	3.09	1.9	1	1.91	0.5	20	15.66	1.3
Rectum	2	1.74	1.1	3	4.01	0.7	3	1.63	1.8	1	0.95	1.1	9	8.32	1.1
Liver, biliary	0	0.44	0.0	1	1.00	1.0	1	0.41	2.5	0	0.25	0.0	2	2.09	1.0
Pancreas	3	0.86	3.5	1	1.98	0.5	3	0.81	3.7	0	0.48	0.0	7	4.13	1.7
Respiratory system	**10**	**5.21**	**1.9**	**22**	**12.28**	**1.8**[b]	**11**	**5.14**	**2.1**[b]	**4**	**2.99**	**1.3**	**47**	**25.60**	**1.8**[b]
Nasal cavities, sinuses	0	0.06	0.0	1	0.13	7.7	0	0.05	0.0	0	0.03	0.0	1	0.27	3.7
Larynx	0	0.58	0.0	0	1.34	0.0	0	0.53	0.0	0	0.29	0.0	0	2.74	0.0
Trachea, bronchus, lung	10	4.53	2.2[b]	21	10.71	2.0[b]	11	4.51	2.4[b]	4	2.64	1.5	46	22.37	2.1[b]
Prostate gland	11	4.99	2.2[b]	26	11.73	2.2[b]	4	4.91	0.8	0	3.16	0.0	41	24.77	1.7[b]
Testis	0	0.05	0.0	1	0.11	9.4	0	0.04	0.0	1	0.02	56.3	2	0.21	9.4[b]
Kidney, renal pelvis, ureter	7	0.65	10.7[b]	2	1.51	1.3	1	0.62	1.6	0	0.36	0.0	10	3.14	3.2[b]
Bladder, other urinary	1	1.93	0.5	4	4.54	0.9	3	1.89	1.6	0	1.16	0.0	8	9.51	0.8
Melanoma of the skin	0	0.28	0.0	3	0.67	4.5	0	0.27	0.0	2	0.15	13.6[b]	5	1.37	3.7[b]
Eye	0	0.04	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.18	0.0
Brain, central nervous system	0	0.27	0.0	2	0.62	3.2	1	0.25	4.0	0	0.13	0.0	3	1.27	2.4
Thyroid gland	0	0.07	0.0	0	0.16	0.0	1	0.06	16.2	0	0.03	0.0	1	0.32	3.1
Bone	0	0.04	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.17	0.0
Connective tissue	0	0.14	0.0	2	0.31	6.5	0	0.12	0.0	0	0.07	0.0	2	0.64	3.1
Lymphatic, hematopoietic system	**0**	**1.80**	**0.0**	**0**	**4.15**	**0.0**[b]	**1**	**1.69**	**0.6**	**1**	**1.01**	**1.0**	**2**	**8.65**	**0.2**[b]
Non-Hodgkin's lymphoma	0	0.56	0.0	0	1.31	0.0	1	0.54	1.9	1	0.31	3.2	2	2.72	0.7
Hodgkin's disease	0	0.13	0.0	0	0.28	0.0	0	0.11	0.0	0	0.06	0.0	0	0.58	0.0
Multiple myeloma	0	0.27	0.0	0	0.63	0.0	0	0.27	0.0	0	0.16	0.0	0	1.33	0.0
Leukemias	0	0.84	0.0	0	1.92	0.0	0	0.78	0.0	0	0.48	0.0	0	4.02	0.0[b]
Chronic lymphocytic	0	0.27	0.0	0	0.63	0.0	0	0.26	0.0	0	0.16	0.0	0	1.32	0.0
Acute nonlymphocytic	0	0.24	0.0	0	0.57	0.0	0	0.24	0.0	0	0.15	0.0	0	1.21	0.0

[a] ICD-O morphology codes = 9800–9940.

[b] $P < .05$.

LEUKEMIA
FEMALES

TABLE 4E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial leukemia among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,849			1,714			545			143			2,849		
Person-yr in interval	1,734			3,863			1,502			580			7,680		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**10**	**13.61**	**0.7**	**41**	**34.15**	**1.2**	**22**	**14.81**	**1.5**	**7**	**6.59**	**1.1**	**80**	**69.11**	**1.2**
All excluding site of initial cancer	**10**	**13.23**	**0.8**	**41**	**33.22**	**1.2**	**22**	**14.41**	**1.5**	**7**	**6.41**	**1.1**	**80**	**67.22**	**1.2**
Buccal cavity, pharynx	**0**	**0.23**	**0.0**	**3**	**0.58**	**5.2**[b]	**1**	**0.26**	**3.9**	**0**	**0.11**	**0.0**	**4**	**1.17**	**3.4**
Lip	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.08	0.0
Tongue	0	0.05	0.0	1	0.12	8.5	0	0.05	0.0	0	0.02	0.0	1	0.24	4.2
Salivary gland	0	0.03	0.0	0	0.08	0.0	0	0.03	0.0	0	0.01	0.0	0	0.15	0.0
Gum, other mouth	0	0.08	0.0	1	0.21	4.9	1	0.09	10.8	0	0.04	0.0	2	0.42	4.8
Pharynx	0	0.05	0.0	1	0.12	8.4	0	0.05	0.0	0	0.02	0.0	1	0.24	4.1
Digestive system	**6**	**4.43**	**1.4**	**21**	**11.19**	**1.9**[b]	**9**	**4.85**	**1.9**	**5**	**2.17**	**2.3**	**41**	**22.63**	**1.8**[b]
Esophagus	0	0.09	0.0	0	0.24	0.0	0	0.11	0.0	1	0.05	21.7	1	0.48	2.1
Stomach	1	0.57	1.8	4	1.41	2.8	1	0.58	1.7	0	0.24	0.0	6	2.80	2.1
Colon	2	2.11	0.9	9	5.36	1.7	3	2.36	1.3	3	1.07	2.8	17	10.89	1.6
Rectum	0	0.83	0.0	5	2.08	2.4	2	0.90	2.2	1	0.40	2.5	8	4.20	1.9
Liver, biliary	2	0.30	6.6	0	0.75	0.0	0	0.32	0.0	0	0.13	0.0	2	1.51	1.3
Pancreas	0	0.45	0.0	1	1.14	0.9	2	0.50	4.0	0	0.23	0.0	3	2.33	1.3
Respiratory system	**1**	**0.79**	**1.3**	**4**	**2.07**	**1.9**	**4**	**0.98**	**4.1**[b]	**1**	**0.45**	**2.2**	**10**	**4.28**	**2.3**[b]
Nasal cavities, sinuses	0	0.02	0.0	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.11	0.0
Larynx	0	0.04	0.0	0	0.11	0.0	1	0.05	18.8	0	0.02	0.0	1	0.23	4.4
Trachea, bronchus, lung	1	0.71	1.4	3	1.88	1.6	3	0.89	3.4	1	0.41	2.5	8	3.89	2.1
Female breast	2	3.38	0.6	8	8.41	1.0	1	3.63	0.3	0	1.59	0.0	11	17.00	0.6
Female genital tract	**0**	**2.06**	**0.0**	**2**	**5.02**	**0.4**	**1**	**2.09**	**0.5**	**0**	**0.90**	**0.0**	**3**	**10.05**	**0.3**[b]
Cervix uteri	0	0.39	0.0	0	0.89	0.0	0	0.33	0.0	0	0.13	0.0	0	1.74	0.0
Corpus uteri	0	0.82	0.0	1	2.07	0.5	0	0.92	0.0	0	0.41	0.0	1	4.21	0.2
Uterus, NOS	0	0.15	0.0	0	0.33	0.0	0	0.11	0.0	0	0.04	0.0	0	0.63	0.0
Ovary, fallopian tubes	0	0.56	0.0	0	1.39	0.0	1	0.58	1.7	0	0.26	0.0	1	2.79	0.4
Kidney, renal pelvis, ureter	0	0.22	0.0	1	0.55	1.8	2	0.24	8.3	0	0.11	0.0	3	1.11	2.7
Bladder, other urinary	0	0.41	0.0	0	1.05	0.0	1	0.47	2.1	0	0.22	0.0	1	2.14	0.5
Melanoma of the skin	0	0.15	0.0	0	0.37	0.0	0	0.16	0.0	0	0.07	0.0	0	0.75	0.0
Eye	0	0.02	0.0	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	0	0.11	0.0
Brain, central nervous system	0	0.13	0.0	0	0.32	0.0	0	0.14	0.0	0	0.06	0.0	0	0.65	0.0
Thyroid gland	0	0.10	0.0	0	0.23	0.0	1	0.09	10.7	0	0.04	0.0	1	0.46	2.2
Bone	0	0.02	0.0	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.10	0.0
Connective tissue	0	0.06	0.0	1	0.15	6.9	0	0.06	0.0	0	0.03	0.0	1	0.29	3.4
Lymphatic, hematopoietic system	**1**	**0.95**	**1.1**	**0**	**2.38**	**0.0**	**0**	**1.04**	**0.0**	**1**	**0.49**	**2.0**	**2**	**4.85**	**0.4**
Non-Hodgkin's lymphoma	0	0.34	0.0	0	0.86	0.0	0	0.39	0.0	1	0.18	5.6	1	1.76	0.6
Hodgkin's disease	0	0.06	0.0	0	0.15	0.0	0	0.07	0.0	0	0.03	0.0	0	0.31	0.0
Multiple myeloma	1	0.17	6.0	0	0.43	0.0	0	0.19	0.0	0	0.10	0.0	1	0.88	1.1
Leukemias	0	0.38	0.0	0	0.93	0.0	0	0.40	0.0	0	0.18	0.0	0	1.89	0.0
Chronic lymphocytic	0	0.11	0.0	0	0.27	0.0	0	0.12	0.0	0	0.06	0.0	0	0.56	0.0
Acute nonlymphocytic	0	0.12	0.0	0	0.31	0.0	0	0.14	0.0	0	0.07	0.0	0	0.64	0.0

[a] ICD-O morphology codes = 9800–9940.

[b] $P < .05$.

ALL
BOTH SEXES

TABLE 5A.– *Characteristics of persons reported to the Connecticut Tumor Registry with an initial acute lymphocytic leukemia, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	501	368	869
No. who developed a second primary cancer	2	3	5
Average age at diagnosis of first cancer, yr	19	20	19
Average yr of diagnosis of first cancer	1967	1966	1967
Person-yr of follow-up	1,090	857	1,947
Average follow-up, yr	2.2	2.3	2.2
Percent given radiotherapy for first cancer	29.7	26.9	28.5

[a] ICD-O morphology codes = 9821–9822.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 5B.– *Microscopic confirmation among persons who developed second primary cancers after an initial acute lymphocytic leukemia in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	4	80.0
Only the first cancer	0	0.0
Only the second cancer	0	0.0
Neither first nor second cancer	1	20.0
Total second primary cancers	5	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

ALL
BOTH SEXES

TABLE 5C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial acute lymphocytic leukemia among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	869			514			124			30			869		
Person-yr in interval	534			949			342			121			1,947		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**0.71**	**2.8**	**2**	**0.79**	**2.5**	**1**	**0.28**	**3.5**	**0**	**0.59**	**0.0**	**5**	**2.36**	**2.1**
All excluding site of initial cancer	**2**	**0.71**	**2.8**	**2**	**0.79**	**2.5**	**1**	**0.28**	**3.5**	**0**	**0.59**	**0.0**	**5**	**2.35**	**2.1**
Buccal cavity, pharynx	**0**	**0.03**	**0.0**	**0**	**0.03**	**0.0**	**1**	**0.01**	**166.1**[b]	**0**	**0.02**	**0.0**	**1**	**0.08**	**13.2**
Lip	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Tongue	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Salivary gland	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Gum, other mouth	0	0.01	0.0	0	0.01	0.0	1	0.00	579.3[b]	0	0.01	0.0	1	0.02	46.1
Pharynx	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Digestive system	**1**	**0.20**	**5.1**	**2**	**0.20**	**10.2**[b]	**0**	**0.08**	**0.0**	**0**	**0.20**	**0.0**	**3**	**0.66**	**4.5**
Esophagus	0	0.01	0.0	1	0.01	103.6[b]	0	0.00	0.0	0	0.01	0.0	1	0.03	33.9
Stomach	0	0.03	0.0	0	0.03	0.0	0	0.01	0.0	0	0.03	0.0	0	0.09	0.0
Colon	1	0.08	12.9	0	0.08	0.0	0	0.04	0.0	0	0.09	0.0	1	0.28	3.5
Rectum	0	0.04	0.0	1	0.04	24.3	0	0.01	0.0	0	0.04	0.0	1	0.13	7.5
Liver, biliary	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.04	0.0
Pancreas	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.07	0.0
Respiratory system	**0**	**0.10**	**0.0**	**0**	**0.11**	**0.0**	**0**	**0.02**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.28**	**0.0**
Nasal cavities, sinuses	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0
Larynx	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.03	0.0
Trachea, bronchus, lung	0	0.08	0.0	0	0.09	0.0	0	0.02	0.0	0	0.05	0.0	0	0.25	0.0
Female breast	0	0.06	0.0	0	0.08	0.0	0	0.05	0.0	0	0.10	0.0	0	0.30	0.0
Female genital tract	**0**	**0.04**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.04**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.19**	**0.0**
Cervix uteri	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Corpus uteri	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.03	0.0	0	0.08	0.0
Uterus, NOS	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Ovary, fallopian tubes	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Prostate gland	1	0.07	14.7	0	0.05	0.0	0	0.00	0.0	0	0.01	0.0	1	0.14	7.2
Testis	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Kidney, renal pelvis, ureter	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Bladder, other urinary	0	0.03	0.0	0	0.03	0.0	0	0.01	0.0	0	0.02	0.0	0	0.10	0.0
Melanoma of the skin	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.03	0.0
Eye	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Brain, central nervous system	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Thyroid gland	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Bone	0	0.00	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.01	0.0
Connective tissue	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.02	0.0
Lymphatic, hematopoietic system	**0**	**0.07**	**0.0**	**0**	**0.10**	**0.0**	**0**	**0.04**	**0.0**	**0**	**0.05**	**0.0**	**0**	**0.26**	**0.0**
Non-Hodgkin's lymphoma	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.07	0.0
Hodgkin's disease	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Multiple myeloma	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.03	0.0
Leukemias	0	0.04	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Chronic lymphocytic	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.02	0.0
Acute nonlymphocytic	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.01	0.0	0	0.04	0.0

[a] ICD-O morphology codes = 9821–9822.

[b] $P < .05$.

CLL
BOTH SEXES

TABLE 6A. —*Characteristics of persons reported to the Connecticut Tumor Registry with an initial chronic lymphocytic leukemia, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,139	736	1,875
No. who developed a second primary cancer	115	50	165
Average age at diagnosis of first cancer, yr	66	69	67
Average yr of diagnosis of first cancer	1967	1968	1967
Person-yr of follow-up	4,724	3,581	8,305
Average follow-up, yr	4.1	4.9	4.4
Percent given radiotherapy for first cancer	19.0	15.4	17.5

[a] ICD-O morphology code = 9823.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 6B. —*Microscopic confirmation among persons who developed second primary cancers after an initial chronic lymphocytic leukemia in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	140	84.8
Only the first cancer	17	10.3
Only the second cancer	6	3.6
Neither first nor second cancer	2	1.2
Total second primary cancers	165	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

CLL
BOTH SEXES

TABLE 6C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial chronic lymphocytic leukemia among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,875			1,522			652			194			1,875		
Person-yr in interval	1,385			4,128			1,896			896			8,305		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**25**	**19.69**	**1.3**	**77**	**60.22**	**1.3**[b]	**46**	**29.44**	**1.6**[b]	**17**	**16.33**	**1.0**	**165**	**125.60**	**1.3**[b]
All excluding site of initial cancer	**25**	**19.49**	**1.3**	**77**	**59.64**	**1.3**[b]	**46**	**29.16**	**1.6**[b]	**17**	**16.16**	**1.1**	**165**	**124.37**	**1.3**[b]
Buccal cavity, pharynx	**0**	**0.74**	**0.0**	**4**	**2.18**	**1.8**	**0**	**1.02**	**0.0**	**1**	**0.55**	**1.8**	**5**	**4.49**	**1.1**
Lip	0	0.13	0.0	0	0.35	0.0	0	0.16	0.0	0	0.09	0.0	0	0.73	0.0
Tongue	0	0.15	0.0	1	0.43	2.3	0	0.20	0.0	1	0.11	9.3	2	0.89	2.3
Salivary gland	0	0.05	0.0	1	0.15	6.8	0	0.07	0.0	0	0.04	0.0	1	0.30	3.3
Gum, other mouth	0	0.21	0.0	1	0.64	1.6	0	0.30	0.0	0	0.16	0.0	1	1.31	0.8
Pharynx	0	0.18	0.0	1	0.53	1.9	0	0.25	0.0	0	0.13	0.0	1	1.09	0.9
Digestive system	**8**	**6.41**	**1.2**	**23**	**19.39**	**1.2**	**18**	**9.43**	**1.9**[b]	**7**	**5.22**	**1.3**	**56**	**40.42**	**1.4**[b]
Esophagus	0	0.32	0.0	0	0.93	0.0	1	0.44	2.3	1	0.24	4.2	2	1.93	1.0
Stomach	2	1.03	1.9	3	2.99	1.0	2	1.40	1.4	1	0.78	1.3	8	6.19	1.3
Colon	1	2.66	0.4	12	8.22	1.5	8	4.07	2.0	4	2.27	1.8	25	17.21	1.5
Rectum	1	1.27	0.8	4	3.84	1.0	2	1.86	1.1	1	1.01	1.0	8	7.97	1.0
Liver, biliary	1	0.36	2.7	1	1.10	0.9	1	0.54	1.9	0	0.29	0.0	3	2.29	1.3
Pancreas	2	0.66	3.0	1	1.99	0.5	4	0.97	4.1[b]	0	0.54	0.0	7	4.15	1.7
Respiratory system	**5**	**2.98**	**1.7**	**15**	**9.15**	**1.6**	**12**	**4.48**	**2.7**[b]	**4**	**2.52**	**1.6**	**36**	**19.12**	**1.9**[b]
Nasal cavities, sinuses	0	0.04	0.0	1	0.12	8.6	0	0.05	0.0	0	0.03	0.0	1	0.24	4.2
Larynx	0	0.30	0.0	0	0.89	0.0	1	0.42	2.4	0	0.22	0.0	1	1.84	0.5
Trachea, bronchus, lung	5	2.61	1.9	14	8.06	1.7	11	3.97	2.8[b]	4	2.25	1.8	34	16.87	2.0[b]
Female breast	0	1.54	0.0	7	5.02	1.4	1	2.58	0.4	0	1.15	0.0	8	10.29	0.8
Female genital tract	**0**	**0.91**	**0.0**	**2**	**2.91**	**0.7**	**0**	**1.45**	**0.0**	**0**	**0.65**	**0.0**	**2**	**5.92**	**0.3**
Cervix uteri	0	0.15	0.0	0	0.47	0.0	0	0.22	0.0	0	0.09	0.0	0	0.93	0.0
Corpus uteri	0	0.38	0.0	1	1.25	0.8	0	0.65	0.0	0	0.29	0.0	1	2.56	0.4
Uterus, NOS	0	0.06	0.0	0	0.17	0.0	0	0.08	0.0	0	0.03	0.0	0	0.34	0.0
Ovary, fallopian tubes	0	0.25	0.0	0	0.82	0.0	0	0.40	0.0	0	0.18	0.0	0	1.65	0.0
Prostate gland	4	2.58	1.6	15	7.72	1.9[b]	3	3.73	0.8	0	2.48	0.0	22	16.50	1.3
Testis	0	0.02	0.0	1	0.05	21.9	0	0.02	0.0	1	0.01	110.6[b]	2	0.09	22.2[b]
Kidney, renal pelvis, ureter	5	0.42	11.8[b]	1	1.29	0.8	2	0.63	3.2	0	0.35	0.0	8	2.69	3.0[b]
Bladder, other urinary	1	1.18	0.8	3	3.60	0.8	4	1.76	2.3	0	1.05	0.0	8	7.58	1.1
Melanoma of the skin	0	0.20	0.0	2	0.63	3.2	0	0.30	0.0	2	0.15	13.0[b]	4	1.28	3.1
Eye	0	0.03	0.0	0	0.08	0.0	0	0.04	0.0	0	0.02	0.0	0	0.17	0.0
Brain, central nervous system	0	0.18	0.0	1	0.55	1.8	0	0.27	0.0	0	0.13	0.0	1	1.12	0.9
Thyroid gland	0	0.07	0.0	0	0.22	0.0	1	0.10	9.5	0	0.05	0.0	1	0.45	2.2
Bone	0	0.03	0.0	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.15	0.0
Connective tissue	0	0.09	0.0	2	0.27	7.3	0	0.13	0.0	0	0.07	0.0	2	0.56	3.5
Lymphatic, hematopoietic system	**1**	**1.33**	**0.7**	**0**	**4.08**	**0.0**[b]	**1**	**2.00**	**0.5**	**1**	**1.12**	**0.9**	**3**	**8.53**	**0.4**
Non-Hodgkin's lymphoma	0	0.44	0.0	0	1.36	0.0	1	0.68	1.5	1	0.36	2.8	2	2.84	0.7
Hodgkin's disease	0	0.08	0.0	0	0.24	0.0	0	0.11	0.0	0	0.06	0.0	0	0.49	0.0
Multiple myeloma	1	0.22	4.5	0	0.69	0.0	0	0.34	0.0	0	0.20	0.0	1	1.45	0.7
Leukemias	0	0.59	0.0	0	1.79	0.0	0	0.87	0.0	0	0.50	0.0	0	3.75	0.0[b]
Chronic lymphocytic	0	0.20	0.0	0	0.58	0.0	0	0.28	0.0	0	0.17	0.0	0	1.23	0.0
Acute nonlymphocytic	0	0.18	0.0	0	0.56	0.0	0	0.28	0.0	0	0.17	0.0	0	1.19	0.0

[a] ICD-O morphology code = 9823.

[b] $P<.05$.

Summary: Multiple Primary Cancers in Connecticut, 1935–82 [1]

Rochelle E. Curtis,[2] John D. Boice, Jr.,[2] Ruth A. Kleinerman,[2] John T. Flannery,[3] *and* Joseph F. Fraumeni, Jr.[4]

ABSTRACT—The risk of developing a second primary cancer was evaluated in over 250,000 persons reported to the Connecticut Tumor Registry (CTR) during 1935-82. The CTR has collected data on cancer incidence longer than any other population-based tumor registry and thus provided researchers with a unique opportunity to investigate the occurrence of second cancers among persons followed for long periods, in some cases for more than 40 years. When compared with the general Connecticut population, cancer patients had a 31% increased risk of developing a subsequent cancer overall and a 23% elevated risk of second cancer at a different site from the first. Little variation in risk was seen for the first 20 years of follow-up, although the risk for females averaged twice that for males (41% vs. 18%). Persons who survived more than 20 years after the diagnosis of their first cancer were at highest risk: 51% for females and 45% for males. Over 1 million person-years of observation were recorded, and the excess risk of developing a new cancer was 3.5 per 1,000 persons per year. Common environmental exposures seemed responsible for the excess occurrence of many second cancers, particularly those related to cigarette smoking, alcohol consumption, or both. For example, persons with epithelial cancers of the lung, larynx, esophagus, buccal cavity, and pharynx were particularly prone to developing new cancers in the same or contiguous tissue throughout their lifetimes. A notable finding was the high risk of cancers of the lung, larynx, buccal cavity, and pharynx observed among cervical cancer patients, which suggested a common etiology involving cigarette smoking. The intriguing association previously reported among cancers of the colon, uterine corpus, breast, and ovary was confirmed in our data, which indicated the possible influence of hormonal or dietary factors. Incidental autopsy findings were largely responsible for the observed excesses of second cancers of the prostate and kidney, and heightened medical surveillance of cancer patients likely resulted in ascertainment bias and elevated risks for some tumors during the early period of follow-up, most notably cancers of the thyroid. Interestingly, patients with prostate cancer were the only ones found to be at significantly low risk for second cancer development. However, this might be an artifact of case-finding because advanced age at initial diagnosis of prostate cancer was associated with an underascertainment of second cancers. Treatment for the first cancer appeared to be responsible for the development of subsequent tumors among patients with cancers of the female genital tract and breast, multiple myeloma, and possibly the lymphomas and leukemias. Radiotherapy may have caused second cancers of the rectum and other sites among patients with cancers of the female genital tract and leukemia among patients with uterine corpus cancer. In addition, chemotherapy probably contributed to the increased risk of acute nonlymphocytic leukemia among patients with multiple myeloma and cancers of the breast and ovary. Large numbers of patients with less common tumors were studied, and high risks of second cancers were found which persisted over time. Genetic susceptibility seemed to explain some excesses of second tumors, such as multiple occurrences of cutaneous melanoma and the development of bone cancer following retinoblastoma. Several new associations were identified as were some possibilities that require further clarification. Through the delineation of multiple cancers, opportunities exist to enhance the understanding of cancer etiology and the implementation of control measures.—Natl Cancer Inst Monogr 68: 219-242, 1985.

The occurrence of multiple primary cancers in particular individuals has intrigued clinicians and scientists for more than a century. The earliest case reports were published in the 1800s (*1*), and since then numerous works have appeared summarizing data that have been collected over many years on simultaneous and metachronous cancers (*2-7*). In the last 30 years, researchers have made considerable progress in determining whether individuals with 1 cancer have an increased, decreased, or unaltered risk of developing a new cancer, either in the same or a different organ. The understanding of multiple cancers was enhanced by the utilization of population-based tumor registries which were able to: 1) identify large numbers of cancer patients for study and thus minimize the significance given to chance occurrence of multiple cancers, 2) avoid the bias inherent in selected populations, such as may occur with patients treated at specialized cancer centers, and 3) provide stable incidence rates derived from the same geographically defined population to make valid comparisons. The CTR, established in 1941 with retrospective reporting of cancers back to 1935, is the oldest such registry in the world. Uniform methods of case ascertainment and histopathologic criteria have been used throughout its 50 years of existence (*8*).

It has long been understood that studies of multiple primary neoplasms provide a strategy for the understanding of the causes of human cancer and for the targeting of programs aimed at reducing carcinogenic exposures and selective cancer screening. Traditionally, studies of multiple cancers have sought to identify associations between 2

ABBREVIATIONS: CTR = Connecticut Tumor Registry; SEER = Surveillance, Epidemiology, and End Results (Program); NHL = non-Hodgkin's lymphoma; CI = confidence interval; RR = relative risk(s); ANLL = acute nonlymphocytic leukemia; NOS = not otherwise specified.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Radiation Epidemiology Branch, Division of Cancer Etiology, Landow Building, Room 3A22, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health and Human Services, Bethesda, Maryland 20892. *Address reprint requests to* Rochelle E. Curtis.

[3] Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut 06106.

[4] Epidemiology and Biostatistics Program, Division of Cancer Etiology.

or more cancers that might provide clues to underlying etiologic factors. The observations are not considered in isolation but in the context of other epidemiologic evidence for tumor relationships (e.g., geographic correlations, familial aggregation) and the available information on risk factors. Many constellations of multiple cancers are associated with the same environmental exposures, whereas others appear to reflect similar endogenous or host factors. Unexplained associations, particularly those that are reciprocal or bidirectional in nature, may generate new hypotheses for future research. The large numbers of rare cancers available from population-based tumor registries, such as the CTR and other SEER registries, provide opportunities for us to study cancers which have few known risk factors or which are uncommon (including heritable syndromes like bilateral retinoblastoma).

The study of treatment-related cancers has become more important during the last two decades, as increasing numbers of cancer patients treated with radiation and chemotherapeutic agents are living longer (*9–13*). Large populations of cancer patients receiving partial body irradiation have been studied extensively so that the differences in organ sensitivities to radiation and their interaction with other biologic factors can be assessed (*14*). Recent surveys of cancer patients have emphasized the leukemogenic properties of therapy with alkylating agents, especially for Hodgkin's disease (*15, 16*), NHL (*17, 18*), multiple myeloma (*19, 20*) and cancers of the ovary (*21, 22*), breast (*13, 23*), lung (*24, 25*), and gastrointestinal tract (*26*). It is not known whether an excess of solid tumors will develop after chemotherapy, similar to the excess observed among long-term survivors of medical or atomic radiation (*27*). To date, only bladder cancer has been reported in excess after chemotherapy, i.e., with chlornaphazine, a drug withdrawn in 1964 as an anticancer agent (*28*), and with cyclophosphamide therapy (*29*).

In 1977, Schoenberg (*4*) made a major contribution to the study of multiple primary cancers by publishing a monograph on the Connecticut experience from 1935 through 1964. Tabulations were included by sex, tumor site, and, in the case of statistically significant associations, by time interval between tumors. Our survey (1935–82) covers an additional 20 years of cancer registration and doubles the number of cancer patients available for evaluation. The person-years at risk for second cancer development are nearly tripled over the previous report. The long follow-up, more than 40 years for some patients, allows us to highlight the risks for long-term survivors. When informative, we have presented data by age and by treatment with or without radiation.

RESULTS AND DISCUSSION

All Cancer Sites

Data from 253,536 Connecticut patients diagnosed with an invasive cancer during 1935 to 1982, who survived at least 2 months without developing a simultaneous primary, were combined so that their collective risk of second primary cancer over time could be examined (tables 1A–1H). More than 1,100,000 person-years of follow-up were accumulated for an average of 4.5 years per person. Both the first and second cancers were microscopically confirmed 88% of the time, providing reasonably good assurance of the reliability of these data. A new primary neoplasm developed in 16,727 (6.6%) patients, whereas 12,797 second cancers were expected on the basis of rates from the general Connecticut population. Thus patients with 1 cancer had 1.31 times the risk (95% CI = 1.29–1.33) of developing a new independent primary compared with Connecticut residents without cancer. This RR is remarkably similar to the 1.29 risk estimate reported from Schoenberg's earlier Connecticut study (1935–64), although almost 20 additional years of cancer diagnoses and follow-up were added to the Connecticut data base. The risk of developing a second cancer was 14.7 per 1,000 persons per year, and the excess risk, i.e., after removing the expected incidence based on population rates, was 3.5 per 1,000 persons per year.

Connecticut residents with cancer remained at increased risk for a new malignant neoplasm throughout their lifetime. Moreover, the risk increased from 1.29 (95% CI = 1.27–1.31) during their first 20 years of follow-up to 1.49 (95% CI = 1.41–1.57) for the 10,297 individuals surviving more than 20 years. Thirty-year survivors (2,218 patients, mostly female) continued to develop new second cancers at a high rate (RR = 1.45, 95% CI = 1.27–1.65). Overall, 3,930 excess cancers developed over what would normally be expected in this population; 1,242 excess cancers (4.6 per 1,000 per yr) developed after 10 or more years of follow-up.

Connecticut cancer patients had significantly elevated risks for second cancers of all subsites in the buccal cavity and pharynx (RR = 1.8), respiratory (1.4) and urinary (1.4) tracts, and for second cancers of the esophagus (1.5), small intestine (2.1), colon (1.3), rectum (1.2), breast (1.9), ovary (1.5), testis (2.0), cutaneous melanoma (1.5), thyroid (1.7), endocrine glands (2.2), bone (1.7), connective tissue (2.0), and ANLL (1.7). Significantly fewer second cancers of the cervix were observed than expected (RR = 0.8). Ten-year survivors experienced especially high risks of second cancers of the buccal cavity and pharynx, colon, rectum, lung, breast, uterus NOS, ovary, kidney, bladder, thyroid, and connective tissue, and ANLL.

These figures are complicated by the inclusion of double primaries involving the same site, particularly the elevated site-specific risks for common initial cancers, such as the colon and breast. To address this issue, we calculated the risks of developing a multiple primary cancer of an organ or tissue different from the first (tables 2A–2C). The risks were based on person-year analyses which excluded patients with an initial cancer at the same site as the second cancer; for example, patients with an initial breast cancer were excluded in the RR calculations for a second breast cancer. For certain organs, cancers of contiguous sites were grouped for exclusion, i.e., for second colon and rectal cancers, patients were excluded with an initial colorectal cancer; for second bladder and kidney cancers, persons with initial urinary cancers were excluded; and for second lip, tongue, and gum/mouth cancers, those with initial oral cavity cancers were excluded. Because the treatment for cancers of the female genital tract frequently eliminates (by surgical ablation) the risk for a second cancer of these organs, these patients were excluded in the risk calculations for second cancers of the female genital sites. Similarly, patients with an initial lymphoma or leukemia were considered not to be at risk for a second lymphoma or leukemia because Registry practices suppressed the recording of these site combinations. After excluding "same site" combinations from the risk estimates, a 23% overall increased risk remained (95% CI = 1.21–1.25), and 2,403 excess cancers occurred at a site different from the first (table 2A). Patients surviving at least 10 years developed 873 excess second cancers (RR = 1.32; 95% CI = 1.28–1.36). Significant RR were then apparent for second cancers of the uterine corpus (1.3) and prostate (1.4). The risk for cervical cancer was no longer decreased, and no cancer of any site occurred significantly below expectation. The results also showed that cancer patients in general were not predisposed to developing second primaries of the stomach, biliary tract, cervix, brain and central nervous system, or any cancer of the lymphatic and hematopoietic system (with the exception of ANLL).

Overall, females were more likely than males to develop a second cancer: RR = 1.42 versus 1.19 (tables 1D, 1E). However, this difference was only apparent in the first 20 years of follow-up; both males and females experienced a 50% increased risk after 20 years of survival (tables 1G, 1H). Second cancers of the breast and gynecologic organs were responsible for a large part of the sex differential in risk. Other sites for which the RR of second cancer was notably higher in women than men included the rectum (1.3 vs. 1.0), lung (1.6 vs. 1.3), bladder (1.4 vs. 1.2), eye (1.8 vs. 1.1), and endocrine gland (2.9 vs. 1.4). The higher RR among women with second cancers of smoking-related sites, such as the lung, may be due to the lower base-line incidence rates for these cancers among females than among males, in combination with the higher frequency of cigarette smoking among cancer patients compared with the general population *(30, 31)*. Only 3 second cancer sites had substantially higher RR for men than for women: thyroid (2.2 vs. 1.5), liver (1.3 vs. 1.0), and a category of "other respiratory" tumors (3.2 vs. 1.5) that includes pleural mesothelioma. The thyroid cancer difference was primarily due to the high risk observed for men within 1 year of diagnosis of the initial primary.

Over 1,000 (25%) of the 3,930 excess second cancers developed at sites strongly linked to use of tobacco or alcohol consumption, or both (table 1C, 1F), notably the buccal cavity and pharynx, esophagus, and respiratory tract. Excess second cancers for these sites have persisted over 30 years since the initial diagnoses, which indicates the need for continued surveillance of long-term survivors.

An excess of 787 second cancers was seen for sites in the lower digestive tract, with significantly elevated RR observed for second cancers of the small intestine (2.1), colon (1.3), and rectum (1.2). The majority of the second colon cancers occurred in patients with an initial colorectal cancer. The remaining excess followed initial cancers of the breast, ovary, and uterine corpus. Excesses of colon cancer increased over time to reach 80% in 20-year survivors. After excluding double colorectal tumors, the rectal cancer excess was highest in long-term survivors of female genital tract cancers treated with radiation.

Over 1,400 excess second breast cancers were observed in females (RR = 1.9); however, 1,291 of these had bilateral breast cancer. After excluding women with an initial breast cancer from analysis, the excess of second breast cancer was 14% overall and 31% for those surviving more than 20 years. The excess was concentrated in patients with initial cancers suspected of sharing a common etiology with breast cancer, particularly cancers of the colon, ovary, uterine corpus, and thyroid, and melanoma. The RR were significantly elevated for second cancers of the uterine corpus (1.3) and ovary (1.6), but not for cervical cancer (1.0), after all patients with initial cancers of the female genital tract were excluded (table 2C). Patients with an initial breast or colon cancer accounted for over 90% of the excess second cancers of the uterine corpus and ovary.

Connecticut cancer patients had a high risk (71%) of developing a second cancer of the kidney, renal pelvis, or ureter. However, an unusually high number of second kidney cancers (102/432 = 24%) were first diagnosed at autopsy or reported only by death certificate compared with 10% for first primary kidney cancers. A large percentage of the excess kidney cancers developed in patients with an initial cancer of the urinary tract, consistent with the multifocal occurrence described for urinary system neoplasms. Elevations of kidney cancer that could not be attributed to incidental autopsy findings were seen following melanoma and cancers of the cervix, uterine corpus, and thyroid. Bladder cancer was diagnosed more frequently than expected after many initial cancers, most notably those in the urinary system and the female genital tract. In long-term survivors, the risk of second bladder cancers remained elevated only in females.

About 25% (316/1,281) of the second prostate cancers were occult tumors detected at autopsy or reported only on a death certificate, in contrast to 10% for first primary prostate cancers. Although the risk of second prostate cancer was elevated after 11 initial tumors, only patients with bladder cancer had a significant excess of second prostate cancer when diagnoses at death were excluded. Six of 19 second testis cancers developed in men with an initial cancer of the testis, which accounted for much of the excess risk for this site.

More than one-half of the excess cases of second melanoma could be explained by the tendency for this cancer to arise at multiple sites in the same person. Much of the elevated risk of subsequent thyroid cancer was concentrated in the first year of follow-up (RR = 3.1), which suggested an observational bias, although moderate increases were also seen in long-term survivors of both sexes. Initial cancers of the breast, uterine corpus, melanoma, and Hodgkin's disease were most often linked to thyroid cancer. A twofold risk for second cancers of connective tissue persisted throughout all follow-up periods and was most prominent following cancers of the breast, ovary, testis, and melanoma, and NHL. A twofold elevation for second endocrine cancer was entirely accounted for by incidental autopsy findings during the first 5 years of follow-up. Second bone cancer was seen with increased frequency overall (77%) and for 10-year survivors. Notable

TEXT-TABLE 1.—*Cancer sites linked to tobacco and excessive alcohol consumption*[a]

Cancer site	Tobacco	Tobacco–alcohol interaction
Lung	+++	No
Larynx	++	Yes
Oral cavity	++	Yes
Pharynx	++	Yes
Esophagus	++	Yes
Kidney	+	No
Bladder	+	No
Pancreas	+	No

[a] *See* (*32, 33*); +++ = strongest association, ++ = strong association, + = moderate to weak association.

excesses of osteosarcoma were observed following cancers of the eye and kidney.

Cancer patients in Connecticut developed NHL and multiple myeloma at the same rate as persons in the general population; however, Hodgkin's disease was observed as a second primary cancer less frequently than expected. Elevations in leukemia, almost entirely due to increases in ANLL, appeared after the first year of observation, remained increased throughout 30 years of follow-up, and were strongly associated with radiation or chemotherapy, or both, for cancers of the breast, ovary, and uterine corpus, and multiple myeloma. Patients with cancers of the lip, prostate, testis, brain, and bladder also developed leukemia more often than expected, but the excesses did not appear related to therapy on the basis of available information.

Upper Digestive and Respiratory Tract Cancers

Among all cancer patients in Connecticut, persons with an initial cancer of the oral cavity, pharynx, or esophagus were at highest risk for developing a new primary cancer especially for sites (text-table 1) related to the multiplicative effects of tobacco and alcohol intake (*32–34*). These persons experienced a more than tenfold excess of second cancers involving the oral cavity, pharynx, or esophagus and a threefold increase of respiratory cancers (text-table 2). Second cancers of the oral cavity frequently developed within the same anatomical or contiguous tissue as the initial cancer, reflecting the tendency of these cancers to be multifocal. Patients with initial cancers of the lip, larynx, and lung experienced a more moderate risk of sites directly exposed to tobacco (RR in the 1.5- to 3.7-range). Excesses of esophageal cancer following laryngeal cancer were probably due to the association of both cancers with excessive alcohol consumption and tobacco smoking. Patients with cancers of the upper digestive and respiratory tracts had only slight increases in risk for more distant cancer sites (bladder and pancreas) related to cigarette smoking. The risk of kidney cancer following lung cancer appeared elevated on the basis of incidental autopsy findings. Excess risks of the smoking- and alcohol-related cancers generally persisted for 10 or more years, were usually higher in women than in men, and appeared in both

TEXT-TABLE 2.—*Significant associations for the development of specific second cancers among patients with initial cancers of the buccal cavity, pharynx, esophagus, and respiratory system, Connecticut, 1935–82*[a]

Tobacco- and alcohol-related associations
Lip <——> lip (4.9)
——> tongue (5.3)
<——> mouth (2.5)
——> larynx (2.5)
——> lung (1.7)
Tongue <——> tongue (9.0)
<——> mouth (16.6)
<——> pharynx (10.7)
<——> esophagus (15.5)
<——> larynx (3.1)
<——> lung (2.9)
Mouth <——> lip (4.8)
<——> tongue (24.0)
<——> mouth (25.1)
<——> pharynx (15.6)
<——> esophagus (12.1)
<——> larynx (4.6)
——> lung (3.2)
Pharynx <——> tongue (17.1)
<——> mouth (12.8)
<——> pharynx (11.4)
<——> esophagus (15.9)
<——> larynx (7.7)
<——> lung (2.9)
Esophagus <——> tongue (14.1)
<——> mouth (9.9)
Larynx <——> tongue (3.7)
<——> mouth (3.1)
<——> pharynx (3.2)
——> esophagus (3.1)
<——> lung (3.2)
Lung <——> tongue (3.0)
<——> pharynx (3.3)
<——> lung (1.5)

Other noteworthy associations
Salivary (4.0) <——> Lung (2.2)
Salivary ——> lip (10.5)
Mouth ——> salivary (12.7)
Mouth ——> nasal cavities (9.3)
Oral cavity, pharynx, larynx ——> digestive tract (all subsites except rectum) especially
tongue ——> stomach (2.2)
mouth ——> colon (1.5)
larynx ——> colon (1.5)
pharynx ——> liver/biliary (3.6)
Nasal cavities ——> lung (5.1)[b]
Lip ——> leukemia (2.1)

Possible artifacts (frequently discovered at autopsy)
Mouth ——> prostate (2.0)
Esophagus ——> prostate (3.5)
Esophagus ——> thyroid (17.2)
Lung ——> prostate (2.0)
Lung ——> kidney (2.6)

[a] First site ——> second site (RR) denotes significantly increased risk (RR are *numbers in parentheses*) of cancer of the second site developing among patients with cancer of the first site. <——> denotes significant RR in both directions. The RR given to the left of <——> is the RR of the first site following second site [e.g., salivary (4.0) <——> lung (2.2) implies that an RR of 4.0 for salivary gland cancers follows lung cancer and an RR of 2.2 of lung cancer follows salivary gland cancer].

[b] The RR is increased for females only.

directions (e.g., tongue cancer was increased after esophageal cancer, and esophageal cancer after cancer of the tongue). These patterns are consistent with previous studies indicating that patients with cancers related to smoking and drinking continue throughout their lifetime to be at high risk of developing a new cancer at the same or neighboring site (*30, 31, 35–39*). The higher RR seen in women as compared with men may be due to the relatively low base-line incidence rates for these cancers among Connecticut women during this period.

Males with salivary gland cancer developed twofold to threefold excess risks for subsequent cancers of the larynx and lung that were also seen in the reverse direction. These bidirectional associations suggest that salivary and respiratory cancers share etiologic factors, although cigarette smoking is not known to cause cancer of the salivary glands (*40*). Earlier reports of an association between cancers of the salivary glands and breast (*41, 42*) were not confirmed in our survey. Despite a recent study implicating tobacco smoking as a risk factor (*43*), cancer of the nasal cavities was not associated with high frequencies of subsequent cancers, either overall or for smoking-related sites. The twofold increase of leukemia subsequent to lip cancer is intriguing and should be explored further.

A small but consistent increase of second cancers of the lower digestive tract, except the rectum, was noted following cancers of the oral cavity, pharynx, and larynx. Primary liver, colorectal, and stomach cancers have been associated with excessive alcohol intake in some studies (*33, 44, 45*), and beer drinking may be specifically related to rectal cancer (*46–48*), but the evidence is not entirely conclusive. Because cancers of the upper digestive system and the respiratory tract appear to be affected by nutritional deficiencies (*33, 49, 50*), dietary factors may contribute to the patterns observed.

TEXT-TABLE 3.—*Significant associations for the development of specific second cancers among persons with an initial cancer of the lower digestive tract, Connecticut, 1935–82*[a]

Multifocal tumors		
Colon	<——>	colon (2.1)
Colon (1.7)	<——>	rectum (1.9)
Common hormonal or dietary risk factors		
Colon (1.2)	<——>	breast (1.2)
Colon (1.4)	<——>	uterine corpus (1.7)
Colon (2.0)	<——>	ovary (2.4)
Small intestine	——>	digestive tract (2.3), especially colon, liver/biliary, pancreas
Possible artifacts frequently discovered at autopsy		
Small intestine	——>	prostate (3.1)
Colon	——>	prostate (1.3)
Rectum	——>	prostate (1.3)
Pancreas	——>	prostate (3.5)
Stomach	——>	kidney (2.2)
Colon	——>	kidney (1.4)
Colon	——>	brain (1.9)[b]
Unexplained or chance associations		
Colon	——>	thyroid (2.9)[c]
Stomach	——>	lymphatic/hematopoietic (2.3),[b] especially ANLL (5.5)
Rectum	——>	pancreas (0.6)
Rectum	——>	stomach (0.7)
Stomach	——>	bladder (1.7)[c]
Liver/biliary	——>	digestive tract (1.9), especially colon, rectum, liver/biliary, pancreas (5.3)

[a] *See* footnote *a* of text-table 2.

[b] The RR is increased for females only.

[c] The RR is increased for males only.

Lower Digestive Tract

Consistent with other studies (*4, 51*), a high risk (RR = 1.7–2.1) of new colorectal cancers occurred after an initial cancer of the colon or rectum (text-table 3). The risk was most pronounced among long-term survivors. Although misdiagnosed metastatic disease might contribute to the excess risk observed during the first 5 years of follow-up, the increasing trend in RR over time suggests that common mechanisms are involved. The demographic patterns of colon and rectal cancers are highly correlated, and many risk factors are shared, including high fat and low fiber diets, high socioeconomic status, inflammatory bowel disease, and genetic or familial syndromes (*52*).

Our survey confirmed previous reports of bidirectional associations between colon cancer and cancers of the breast, uterine corpus, and ovary (*51, 53, 54*). However, the overall risk of second breast cancer was small (20%), and the increased incidence of second ovarian cancer may be an artifact. The ovary is a common metastatic site for colon cancer (*55*), and the risk elevation was confined to the first 5 years postdiagnosis. The excesses of breast and uterine corpus cancer following colon cancer were highest in 10-year survivors. Positive geographic correlations have been noted among mortality rates for breast, colon, uterine corpus, and ovarian cancers (*56, 57*). Case–control studies have also revealed an increased risk of colon, but not rectal, cancer associated with low parity and nulliparity (*58, 59*), which are well-established risk factors for breast, uterine corpus, and ovarian cancers. These characteristics suggest that hormonal factors combined with nutritional status may underlie this constellation of tumors (*53, 60*). Inasmuch as familial syndromes of cancer may encompass these particular neoplasms, it is possible that genetic factors contribute to this pattern of multiple primaries (*61*).

Colon cancer patients were also at high risk for second cancers of the prostate, kidney, and thyroid among males and brain cancers among females. However, most of these excesses were attributable to a high proportion of second primaries diagnosed at autopsy. Increased medical surveillance may also be involved in the thyroid excess in males because one-third of the tumors were diagnosed within the first year after diagnosis.

Although based on small numbers, patients with cancer of the small intestine had an elevated risk of developing second digestive cancers, mainly of the large bowel, liver and biliary tract, and pancreas. International studies have revealed geographic correlations between cancers of the colon and small intestine, which suggest a common etiology possibly related to diet (*62*). In addition, a significant excess of digestive cancers was observed following cancers of the liver and biliary tract, with an eightfold risk of subsequent pancreatic cancer among males being most noteworthy. Bile duct and pancreatic cancers may have shared risk factors (*63*), but misdiagnosed metastatic spread may complicate interpretation of these findings. Among stomach cancer patients, elevations were seen for subsequent bladder cancer in males and ANLL among females.

It is interesting that patients with initial cancers of the lower digestive tract did not develop excess risks for second cancers of the major tobacco- and alcohol-related sites (oral cavity and pharynx, larynx, lung, and esophagus), although a positive association was seen in the opposite direction. Rectal cancer has been associated with excessive beer drinking in some studies (*46–48*), but patients with this tumor were not prone to any second cancers traditionally associated with heavy alcohol consumption. An excess of lung cancer was not seen after pancreatic cancer, both smoking-related tumors, probably because of the poor survival experience associated with pancreatic cancer.

TEXT-TABLE 4.—*Significant associations for the development of specific second cancers among females with an initial cancer of the breast or female genital tract, Connecticut, 1935–82*[a]

Multifocal tumors		
Breast	<——>	breast (3.0)
Common etiology: Hormonal or dietary risk factors		
Breast (1.3)	<——>	uterine corpus (1.4)
Breast (1.4)	<——>	ovary (1.7)
Breast (1.9)	<——>	thyroid (1.6)
Breast (1.2)	<——>	colon (1.2)
Breast (1.5)	<——>	melanoma (1.5)
Breast	——>	eye (melanoma) (2.5)
Uterine corpus (1.7)	<——>	colon (1.4)
Uterine corpus	——>	thyroid (2.0)
Ovary (2.4)	<——>	colon (2.0)
Ovary	——>	uterine corpus (1.6)
Smoking related		
Cervix	——>	buccal cavity and pharynx (2.4)
Cervix	——>	larynx (5.7)
Cervix	——>	lung (3.4)
Possibly treatment related		
Cervix (radiation)	——>	kidney (3.4)[b, c]
	——>	bladder (5.0)[b, c]
	——>	rectum (3.0)[b]
	——>	ovary (1.8)[b]
	——>	breast (0.7)
Uterine corpus (radiation)	——>	rectum (2.0)[b]
	——>	ANLL (2.4)
	——>	multiple myeloma (2.0)[c]
Ovary (radiation)	——>	colon (2.6)[b, c]
	——>	rectum (3.5)[b]
	——>	connective tissue (24.6)[b]
	——>	bladder (7.2)[b, c]
Ovary (chemotherapy)	——>	ANLL (43.0)
Breast (radiation)	——>	connective tissue (4.2)[d]
	——>	NHL (1.7)
	——>	lung (2.8)[b]
	——>	ANLL (2.5)[e]
Unexplained or chance associations		
Breast (1.4)[f]	——>	lung (1.3)
Breast	——>	multiple myeloma (0.5)
Breast (radiation)	——>	kidney (1.9)
Uterine corpus	——>	lung (1.4)
Uterine corpus	——>	kidney (2.1)
Uterine corpus	——>	bladder (1.7)
Ovary	——>	kidney (2.8)[g]

[a] *See* footnote *a* of text-table 2.

[b] The RR is given for irradiated patients, 10+ yr follow-up interval.

[c] Elevated risks were seen for this site pair in the first 5 yr of follow-up that are unlikely to be related to radiation treatment.

[d] Increased risk may also be related to lymphedema from radical mastectomy.

[e] Chemotherapy may also increase risk of ANLL following breast cancer.

[f] The RR is not significant ($P > .05$).

[g] Second kidney cancer after ovarian cancer was frequently diagnosed at autopsy.

Breast and Female Genital Organs

Second breast cancer was diagnosed in 1 of 20 (5%) women with a first primary breast cancer and in 1 of 14 (7%) women whose initial breast cancer was diagnosed under age 45. A threefold risk of second breast cancer was observed overall (text-table 4). Although decreasing with time, the risk remained elevated after 30 years of follow-up. Bilateral breast cancer has been shown to occur at higher rates than expected (*64–67*), with hormonal and genetic determinants suspected to be involved. The fivefold risk among younger women is notable because it may reflect more aggressive disease or the tendency for familial cases to develop at a younger age (*68*). The data were examined by treatment, and no clear evidence for an effect of radiotherapy on second breast cancer risk was seen.

Previous studies (*65, 69–74*) have indicated that hormonally related risk factors may explain the two-way association observed between breast cancer and cancers of the uterine corpus and ovary, but the specific mechanisms involved have not been identified. These 3 cancers share certain risk factors, such as nulliparity, which suggests a hormonal predisposition (*53, 74–76*). The early excess of ovarian cancer following breast cancer could represent mistaken metastases (*55*), although this is an unlikely explanation for the increased incidence in long-term survivors. Hormonal factors may also apply to colon cancer, which showed bidirectional associations with tumors of reproductive sites, although common dietary factors could also be involved.

A deficit of breast cancer was seen following cervical cancer (RR = 0.8), which remained constant over all follow-up intervals. This result was anticipated, inasmuch as the risk factors associated with 1 cancer tend to be protective for the other (*53*). However, the decreased risk of subsequent breast cancer was confined to women treated with radiotherapy (RR = 0.7). Studies of surgically induced menopause have noted a 5- to 10-year latency before reduction in breast cancer risk becomes evident (*77*); however, radiation ablation of the ovaries may have been associated with a protective effect even before this period.

Reproductive or hormonal factors might also be related to the reciprocal association seen between cancers of the breast and thyroid (*78*) and between breast cancer and malignant melanoma (*79*). Thyroid cancer was also elevated following uterine corpus cancer, but no excess risk was seen in the reverse direction.

Patients with cervical cancer had threefold to fourfold risks of developing second cancers of various tobacco-related sites (oral cavity and pharynx, esophagus, and respiratory tract). There was also some increased RR of cervical cancer following lung cancer (2.0), although only 4 cases were observed. The link between cigarette smoking and cervical cancer was first suggested on the basis of concomitant geographic variation (*80*) and has since been supported by case-control studies (*81, 82*). Although some investigators suggest that this association is confounded by the relationship between smoking and other risk factors for cervical cancer, such as low socioeconomic status (*83*), the large risks found in this study are unlikely to be accounted for by socioeconomic factors. Thus our findings suggest that lung and cervical cancers may share a common risk factor, probably cigarette smoking.

The increase in second lung cancer following initial cancers of the breast, uterine corpus, and ovary was not anticipated because previous studies have not linked cigarette smoking to the hormonally related cancer sites (*84, 85*). The lung cancer excesses were of lower magnitude (30–60%) than those seen for cervical cancer, and they were not matched by elevations in second cancers of other smoking-related sites. Interestingly, nonsignificant elevations of second neoplasms of the ovary and breast (40%) were seen following lung cancer. Radiation might have influenced the lung cancer risk in long-term survivors of breast cancer (*27*), inasmuch as the lung is heavily exposed during radiotherapy. However, nonexposed women also had an elevated risk of developing a subsequent lung neoplasm. Because the lung is a common metastatic site for breast cancer, misdiagnosed metastases may also contribute to the patterns observed.

An increased incidence of second cancer of the abdominal organs (colon, rectum, kidney, bladder, ovary, and uterine corpus) was generally observed for each gynecologic site. However, only rectal cancer was consistently linked with pelvic irradiation. In each instance, threefold excesses of rectal cancer developed after 10 to 20 years of follow-up, and the increased risks were confined to women treated with radiotherapy. These results are consistent with the relatively long latent period observed for radiation-induced solid tumors and with other studies of pelvic irradiation (*14, 27*). Radiation treatment for cervical cancer also may have contributed to the increase of second ovarian cancer occurring after 30 years of follow-up, as well as a portion of the excess kidney and bladder cancers in long-term survivors. The twofold to threefold excess of second bladder and kidney cancers following uterine corpus and ovarian cancers did not appear related to treatment. Elevated risks were not seen for second cancers of the female genital sites following either kidney or bladder cancer. Because all patients with gynecologic cancer undergo frequent monitoring for metastatic spread to the pelvic organs or recurrence of the initial cancer, these excesses may result at least partly from a medical surveillance bias.

The significantly elevated risk of bone cancer after uterine corpus cancer and the excess of connective tissue cancers after breast and ovarian cancers also might be related to radiation therapy. Bone and connective tissue cancers can be induced by high-dose radiation (*27, 86*), and the excess risks were concentrated in long-term survivors who received radiotherapy for their initial cancer. Some of the soft tissue sarcomas appearing after breast cancer were lymphangiosarcomas which have been reported following lymphedema of the upper extremities complicating radical mastectomy (*87*).

Cervical cancer patients who have received partial body exposure to high-dose radiation (3,000–7,000 rad) have been extensively studied, and large excesses of leukemia have not been reported (*14, 88*). High doses of radiation to small volumes of bone marrow have been thought to inactivate the cells, as well as to transform them, thereby reducing the number available for cancer induction (*14*). Therefore, it is noteworthy that a twofold excess of leukemia was observed following radiotherapy for cancer of the uterine corpus. This finding is contrary to a previous report by Wagoner (*89*) based on earlier Connecticut data (1935–64), but it is consistent with the risks found more recently among patients reported to 9 SEER tumor registries (*13*). The excess of ANLL developing in ovarian cancer patients was expected because previous reports have described this risk associated with the use of alkylating agents (*21*). Breast cancer patients receiving radiation treatment also had an elevated ANLL risk; however, the increase may be due to the initiation of adjuvant chemotherapy in the mid-1970s for patients with regional node involvement (*13, 23, 90, 91*).

Male Genital System

Men with prostate cancer were at significantly low risk of developing a second primary cancer throughout all follow-up intervals. Substantial deficits were evident for subsequent cancers of the esophagus, stomach, colon, and lung (text-table 5). Reduced medical surveillance in this primarily elderly population (average age = 72 yr) might account for these findings because deficits were generally not seen for patients diagnosed under age 65. Only salivary gland cancer was in excess, possibly a chance association. An excess of leukemia (RR = 1.3) was of borderline significance and not associated with radiotherapy.

In contrast to prostate cancer, men with testis cancer experienced a twofold risk of second cancers over all follow-up intervals and in both irradiated and nonirradiated groups. Bidirectional associations with leukemia and NHL were observed, although the number of cases was small. A significant risk of leukemia following testis cancer has been reported (*92*). In our series, high risks of

TEXT-TABLE 5.—*Significant associations for the development of specific second cancers among men with initial cancer of the male genital system, Connecticut, 1935–82*[a]

Multifocal tumors		
Testis	<——>	testis (11.2)
Possible common etiologic factors		
Testis (9.4)	<——>	leukemia (5.2)[b]
Possible artifacts due to reduced medical surveillance		
Prostate	——>	esophagus (0.5)
Prostate	——>	stomach (0.7)
Prostate	——>	colon (0.9)
Prostate	——>	lung (0.7)
Prostate	——>	brain, central nervous system (0.2)
Prostate	——>	mouth (0.5)
Unexplained or chance associations		
Testis	——>	pancreas (3.9)
Testis	——>	prostate (2.0)
Testis	——>	kidney (3.3)
Testis	——>	NHL (4.1)
Testis	——>	bladder (2.6)
Testis	——>	connective tissue (8.6)
Prostate	——>	salivary gland (2.7)
Prostate	——>	leukemia (1.3)[c]

[a] *See* footnote *a* of text-table 2.

[b] A portion of increased RR of testis ——> ANLL may be due to chemotherapy treatment introduced for testis cancer in the 1970s (2 of 5 patients received drug therapy).

[c] The RR has borderline significance ($P = .05$).

leukemia were seen in both irradiated and nonirradiated groups. Successful chemotherapy treatment was introduced for this cancer in the early 1970s, so that some ANLL cases may have been drug induced. There were also excess risks for cancers of the contralateral testis and for second cancers of the pancreas, kidney, bladder, and connective tissue, which cannot be readily attributed to treatment or other risk factors.

Urinary System

Patients with an initial cancer of the bladder or kidney (including renal pelvis or ureter) were prone to second cancers of the urinary tract. Increased risks were fivefold for bladder cancer following kidney cancer and sevenfold for kidney cancer after bladder cancer (text-table 6). The multifocal nature of transitional cell cancers of the lower urinary tract (renal pelvis, ureter, and bladder) appears to reflect a "field change" phenomenon caused by exposure of the urothelial surface to tobacco and other carcinogens, possibly combined with unusual host or tissue susceptibility (*93, 94*). To some extent, increased medical surveillance also may have contributed to this risk. Bladder cancer patients were also prone to lung and laryngeal cancers, presumably due to relationships with cigarette smoking. The unusual excess of ANLL and NHL seen among male bladder cancer patients suggests the possible influence of occupational exposure or an effect of treatment (radiotherapy or chemotherapy).

Cutaneous Melanoma, and Cancers of the Brain, Thyroid, Connective Tissue, Bone, and Eye

Individuals with cutaneous melanoma were at exceptionally high risk of developing second melanoma at a different location (text-table 7). Excess risks surpassing twentyfold were found for persons under age 40 at the time of original melanoma diagnosis, which suggests a hereditary component (*95*). The association of melanoma with breast cancer in both directions and with subsequent cancers of the colon, thyroid, and uterine corpus (although the latter association did not reach statistical significance) is provocative given the purported, but controversial, role of estrogens in the development of melanoma (*96, 97*). Also interesting is the sevenfold excess of subsequent connective tissue tumors; a follow-up histologic review indicated that 6 of 7 cases were not obviously metastatic melanoma (Greene MH, Flannery JT, Clark WH Jr: Personal communication). An enhanced ANLL risk following melanoma in men raises the possibility of a treatment effect because many of these patients would have received radiation, chemotherapy, or both.

Both melanoma and ANLL occurred in excess following brain cancer. The increased risk of melanoma may reflect an underlying developmental defect in the neural crest (*98*); melanoma metastatic to the brain is an unlikely explanation because 3 of the 4 melanomas were diagnosed at least 3 years after the initial brain tumor. Chemotherapy given for the brain tumor may be related to the increase in ANLL.

We previously noted that thyroid cancer was diagnosed more frequently than expected after breast and uterine corpus cancers, so that the excess of breast cancer after thyroid cancer suggests common etiologic factors. How-

TEXT-TABLE 6.—*Significant associations for the development of specific second cancers among persons with initial cancers of the urinary system, Connecticut, 1935–82*[a]

Transitional cell multicentric tumors		
Kidney (4.6)	<——>	bladder (6.9)
Kidney	<——>	kidney (2.9)
Smoking related		
Bladder	——>	lung (1.5)
Bladder	——>	larynx (1.7)
Kidney	——>	lung (2.2)[b]
Possibly therapy related		
Bladder	——>	NHL (1.6)[c]
Bladder	——>	ANLL (2.2)[c]
Unexplained or chance associations		
Bladder	——>	bone (4.3)[c]
Kidney	——>	esophagus (0.0)
Possibly artifacts frequently discovered at autopsy		
Bladder	——>	prostate (1.6)[d]
Kidney	——>	prostate (1.5)
Kidney	——>	bone (9.0)

[a] *See* footnote *a* of text-table 2.

[b] The RR is increased for females only.

[c] The RR is increased for males only.

[d] The RR remained significantly elevated (1.4) after exclusion of second cancers of the prostate diagnosed at autopsy.

TEXT-TABLE 7.—*Significant associations for the development of specific second cancers among persons with initial cancer of the eye, connective tissue, bone, brain and central nervous system, and melanoma, Connecticut, 1935-82*[a]

Multifocal tumors, genetic susceptibility		
Melanoma	<——>	melanoma (8.5)
Thyroid	<——>	thyroid (4.7)
Eye	<——>	eye (24.1)[b]
Eye	——>	bone (35.7)[c]
Suggestive of common risk factors		
Melanoma (1.5)	<——>	breast (1.5)
Melanoma	——>	colon (1.4)
Melanoma	——>	thyroid (3.6)
Thyroid (1.6)	<——>	breast (1.9)
Brain	——>	melanoma (6.1)
Possibly therapy related		
Brain	——>	ANLL (10.1)
Bone (15.4)	<——>	connective tissue (16.4)
Melanoma	——>	ANLL (3.9)[d]
Unexplained or chance associations		
Melanoma	——>	kidney (2.2)
Melanoma	——>	lung (2.5)[e]
Melanoma	——>	connective tissue (6.9)
Thyroid	——>	kidney (4.8)
Thyroid	——>	connective (5.4)
Thyroid	——>	pancreas (3.4)[e]
Thyroid	——>	larynx (8.0)[e]
Eye	——>	lung (2.5)
Eye	——>	uterus NOS (11.9)
Bone	——>	lymphatic/hematopoietic (3.4)
Possible artifact		
Connective tissue	——>	connective tissue (6.3)

[a] *See* footnote *a* of text-table 2.

[b] Excess risks are due to bilateral retinoblastoma.

[c] Elevated risk of retinoblastoma ——> osteosarcoma also may be related to radiation.

[d] The RR is increased for males only.

[e] The RR is increased for females only.

ever, these tumors appear dissimilar in hormonal and reproductive associations (*99*). Patients with thyroid cancer had a fourfold excess of kidney cancer in both sexes; this association was unidirectional and could not be explained by incidental autopsy findings.

Among patients with cancer of connective tissue, the risks for second bone and connective tissue cancers were elevated. Bone cancer may be therapy-related because it has been reported after radiation treatment for soft tissue sarcomas in young children (*100*). Studies of sarcoma-prone families suggest the influence of genetic susceptibility to spontaneous and radiogenic sarcomas (*101*). However, the increase in second primaries of the connective tissues may partly reflect metastatic disease, given the difficulties involved in accurate diagnosis of multiple tumors of this type (*102*).

Although an overall significant risk of a patient developing a second primary was observed after the diagnosis of bone cancer, the results for individual sites were based on small numbers. Two patients developed connective tissue tumors, which may have been radiation induced (*86*). An anticipated excess of second bone cancer was not observed, despite reports of radiogenic osteosarcoma following Ewing's sarcoma (*100, 103*) and the tendency of some patients to have multifocal osteosarcomas (*104*).

An analysis of patients with eye cancer by age revealed that children had a high risk of developing second eye and bone cancers. The first association is due to bilateral retinoblastoma, a dominantly inherited neoplasm (*105*). The second association reflects the high rate of osteosarcoma following hereditary retinoblastoma. The bone tumors may arise in the orbital radiation field or in the lower extremities as a pleiotropic manifestation of the retinoblastoma gene (*100*). Adults with eye cancer (usually melanoma) also had an increased RR of subsequent primaries (1.3), but except for lung cancer, the excesses were confined to the first 5 years of follow-up and may have resulted from observational bias.

Lymphatic and Hematopoietic Systems

Among patients with Hodgkin's disease, excess second cancers were concentrated in the buccal cavity and lung among men, and the lung, breast, and thyroid among women (text-table 8). The threefold risks for cancers of the lung and buccal cavity suggest a smoking effect, but there is no evidence to suggest that Hodgkin's disease is smoking related. The excess cancers of the lung, breast,

TEXT-TABLE 8.—*Significant associations for the development of specific second cancers among persons with an initial cancer of the lymphatic or hematopoietic system, Connecticut, 1935-82*[a]

Possibly related to immunosuppression		
Leukemia	——>	melanoma (3.7)[b]
NHL	——>	melanoma (3.1)[b]
Possibly radiotherapy related[c]		
Hodgkin's disease	——>	breast (3.0)[d]
Hodgkin's disease	——>	thyroid (6.7)
Hodgkin's disease	——>	lung (5.5)[d]
Hodgkin's disease	——>	buccal cavity, pharynx (3.1)
NHL	——>	connective tissue (5.0)
NHL	——>	stomach (2.8)[d]
Chemotherapy related		
Multiple myeloma	——>	ANLL (16.0)
Possible common etiologic factors		
Leukemia (5.2)	<——>	testis (9.4)
Unexplained or chance associations		
Leukemia	——>	lung (2.1)
Leukemia	——>	colorectal (1.4)
Leukemia	——>	female genital (0.3)
NHL	——>	lung (1.9)
NHL	——>	brain (3.1)
Possible artifacts frequently discovered at autopsy		
Leukemia	——>	prostate (1.7)
Leukemia	——>	kidney (3.1)

[a] *See* footnote *a* of text-table 2.

[b] The RR is increased for males only.

[c] Past reporting practices in Connecticut prevent an assessment of the risk of subsequent ANLL or lymphoma in patients with a first primary Hodgkin's disease or NHL.

[d] The RR is given for 10+ yr follow-up interval, all treatments.

and thyroid might be related to radiotherapy because the highest risks occurred in 10-year survivors. Second lung cancer also developed in excess following NHL and leukemia, although the risks were smaller in magnitude and changes with follow-up were not evident. Several reports have linked lung cancer with lymphomas (*17*), which suggests that defective immunity could predispose to lung cancer as observed in renal transplant recipients (*106*).

An excess of cutaneous melanoma, confined to males, was found in NHL and leukemia patients. Although based on small numbers, the finding is consistent with previous reports relating immunosuppression with melanoma development (*107*). The excess of stomach cancers following NHL is consistent with case reports (*108*) and may be related to radiation treatment (*27*) or to immune defects as seen in immunologically compromised patients (*106, 109, 110*). Immune defects (*107*) and radiation therapy may have contributed to the increased risk of connective tissue cancer seen following NHL. Brain cancer was significantly elevated after NHL, but it is possible that some cases were actually brain lymphomas (also referred to as microgliomas) and not second primaries.

We could not confirm previous reports of a high risk of ANLL after Hodgkin's disease (*16*) or NHL (*17*). Krikorian et al. (*111*) found that NHL was elevated after treatment for Hodgkin's disease, which had been related to altered immunity. Past reporting and coding practices in Connecticut did not record leukemias or lymphomas developing in patients with an initial lymphoma (*13*). The data were sufficient, however, for us to detect an unusually high risk of ANLL following multiple myeloma (RR = 16.0), which has been attributed to therapy with alkylating agents (*19, 112*).

CONCLUSIONS

The study of multiple primary cancers has been facilitated by the maturation of population-based tumor registries so that large numbers of cancer patients from a well-defined population can be followed for many decades and the risk of a second primary cancer can be accurately quantified. The CTR, with more than 350,000 cancers and almost 50 years of follow-up, has proved to be an invaluable resource in identifying associations between 2 (or more) cancers and in clarifying the patterns of risk over many years of follow-up. Consistent with an earlier Connecticut survey (*4*), our study revealed that patients with 1 cancer had a 31% overall increased risk of developing a second primary cancer. Although the tendency toward a multifocal origin for specific cancers is well known, persons with 1 cancer of a particular organ also had a significantly increased risk (23%) of developing a new cancer in a different organ or tissue.

A major contribution of this monograph is the evaluation of second cancer risk among long-term survivors. Over 10,000 Connecticut residents were followed for 20 or more years, and follow-up data were accumulated for 2,200 persons for at least 30 years. Long-term survivors appeared particularly prone to developing a new subsequent cancer; the risk increased to 49% for those who survived more than 20 years after the diagnosis of their first cancer. Thus cancer patients must be continually monitored for the development of a new neoplasm throughout their lifetime.

A substantial number of the multiple primary cancers could be attributed to underlying environmental exposures, particularly cigarette smoking and alcohol consumption as risk factors for multiple cancers of the upper digestive and respiratory tracts. In addition, the intriguing associations among colon, uterine corpus, breast, and ovary cancers were confirmed in these data, which suggest the role of endogenous hormones or dietary factors yet to be elucidated. Incidental autopsy findings elevated the risk of second cancers of the prostate and kidney following 11 primary sites, and diagnostic surveillance played a role, particularly in raising the risk of tumors in the same organ system. Treatment for cancers of the breast, female genital tract, and multiple myeloma, and possibly the lymphomas and leukemias, appeared to increase the risk of subsequent cancers. In contrast to many previous studies, sizable numbers of patients with usually rare cancers were followed for long periods, with detection of increased second cancer risks that have persisted over time. The association between eye and bone cancers reflected the inherited syndromes of retinoblastoma and osteosarcoma and illustrates the importance of family or pedigree studies to clarify genetic mechanisms underlying some constellations of cancer. Finally, several new associations were identified in our study that seem provocative and warrant further investigation.

In evaluating our results, the reader should take care to distinguish real from spurious findings. Statistically significant associations, observed in both directions and occurring at a relatively constant rate over time, constitute strong evidence that 2 cancers possess common etiologic factors. However, it is difficult sometimes for one to distinguish metastatic disease from an independent primary cancer, particularly when the cancers share epithelial tissues in close proximity to one another, or when the second cancer is a common site for metastatic spread, such as the lung, brain, or bone. The results are particularly suspect when the microscopic confirmation rate for both primaries is low. On the other hand, a new cancer that develops shortly after the occurrence of the first primary might incorrectly be assumed to be a metastatic lesion and not considered as a possible new primary. The Connecticut data, in fact, provide some evidence of a possible underreporting for common metastatic sites, e.g., second lung cancers occurred less frequently than expected during the first year of follow-up (RR = 0.8, all cancer sites combined).

Observational bias may affect results in multiple primary studies because patients with 1 cancer are likely to be under closer medical surveillance than persons in the general population. During the first 5 years of follow-up, when patients are at highest risk for a recurrence or metastases and are most closely followed, medical scrutiny could result in the detection of occult tumors, the advancement in time of the diagnosis of some cancers, or the misclassification of a metastatic lesion. One example of a likely observational bias is the threefold elevation in second thyroid cancer risk that occurred during the first year of follow-up for all initial cancer sites combined. Risk estimates can also be misleading if the percentage of second cancers diagnosed at autopsy (or reported only by death certificate) is substantially higher than what might be expected in the general population. In the Connecticut series, most excesses of second kidney and prostate cancers were attributable to incidental autopsy findings. High frequencies of second cancers reported at autopsy were also noted for second cancers of the thyroid, liver, pancreas, and endocrine organs. Finally, in any analysis which involves a large number of comparisons, one can expect spurious associations to develop based on chance alone.

It is important that our findings be compared with results based on other data sources. Of special value will be the population-based cancer registries (including Connecticut) participating in the SEER Program (*113*). Currently, the SEER registries have more than a decade of cancer registration and follow-up on a population encompassing close to 12% of the residents in the United States. One could use these data to explore racial and ethnic differences in second cancer risk, study rare sites in greater depth, and to evaluate risks by histologic type where appropriate. Case-control studies of patients selected from these and other populations could also be conducted for further exploration of the findings from the Connecticut survey.

Future studies should emphasize the surveillance of therapy-related tumors in view of major advances in cancer treatment, notably chemotherapy, during the 1960s and 1970s. We will need a combination of descriptive and analytic studies to identify the particular drugs and drug combinations that may be harmful. As long-term survivors of these therapies become available for study in increasing numbers, the risk of second primary solid cancers must be systematically evaluated in light of the high rates of ANLL found in many series following chemotherapy. Of particular interest are the survivors of cancers affecting young people because the progress in treatment has been especially pronounced in this group.

Although a substantial body of evidence is available on the effects of radiotherapy for nonmalignant disease, further work is required for an evaluation of the carcinogenic risks of high-dose partial body radiation. Many questions remain concerning the dose-response relationships for specific organs, the relationship to age at exposure, the effect of specific types of radiotherapy, such as radioisotopes or megavoltage x-ray beams, and the effect of fractionated doses in causing tumors. Wherever possible, the interaction of radiation with other exposures (e.g., chemotherapy) and host factors should be evaluated. In our study, several risks were identified that require further research to clarify the role of radiotherapy. These include the following: the high rate of leukemia and cancers of the pelvic organs, bone, and connective tissue among patients treated with radiation for uterine corpus and ovarian cancers; the effect of radiotherapy for Hodgkin's disease on the risk of second cancers of the lung, buccal cavity, breast, and thyroid, and for NHL on subsequent cancers of the stomach and connective tissue; and possible treatment effects in the excess of ANLL following cancers of the testis, bladder, breast, and brain, and melanoma.

In summary, the findings from the Connecticut survey have expanded our knowledge about the patterns of multiple primary cancers, especially among long-term survivors. As the complexes of multiple tumors become more clearly delineated, attention should turn to the identification of risk factors, which are likely to have broader implications for cancer etiology and mechanisms of carcinogenesis. Because a number of risk factors may elude the traditional approaches of epidemiology and clinical genetics, the incorporation of laboratory techniques should help derive information that could not be developed by epidemiology or experimental study alone. In studies of multiple cancers, the laboratory aspect may increase our ability to define carcinogenic exposures, preclinical responses and precursor states, susceptibility mechanisms, and host-environmental interactions. Experimental probes are increasingly useful, e.g., in clarification of the role of nutritional influences, endocrine profiles, infectious agents, immunocompetence, or genetic markers (including oncogenes) that may be critical to the development of multiple cancers. With advances in our understanding of multiple cancer syndromes, benefits will accrue not only to etiologic research, but also to cancer prevention and detection programs aimed at high-risk individuals.

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ALL CANCER SITES
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Connecticut Tumor Registry with any first primary cancer, 1935–82*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	120,253	133,283	253,536
No. who developed a second primary cancer	7,507	9,220	16,727
Average age at diagnosis of first cancer, yr	63	60	61
Average yr of diagnosis of first cancer	1966	1965	1965
Person-yr of follow-up	409,878	725,846	1,135,724
Average follow-up, yr	3.4	5.4	4.5
Percent given radiotherapy for first cancer	29.5	32.0	30.8

[a] ICD-O codes = 140–199.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after any first primary cancer in Connecticut, 1935–82*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	14,735	88.1
Only the first cancer	1,428	8.5
Only the second cancer	439	2.6
Neither first nor second cancer	125	0.8
Total second primary cancers	16,727	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

ALL CANCER SITES
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males and females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	253,536			168,934			74,431			36,969			253,536		
Person-yr in interval	165,884			433,121			263,868			272,851			1,135,724		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2,286**	**1,785**	**1.3**[b]	**6,035**	**4,693**	**1.3**[b]	**3,795**	**2,958**	**1.3**[b]	**4,611**	**3,369**	**1.4**[b]	**16,727**	**12,797**	**1.3**[b]
Buccal cavity, pharynx	**126**	**64**	**2.0**[b]	**292**	**159**	**1.8**[b]	**167**	**93**	**1.8**[b]	**153**	**91**	**1.7**[b]	**738**	**407**	**1.8**[b]
Lip	16	10	1.5	32	25	1.3	22	14	1.6	23	12	1.9[b]	93	61	1.5[b]
Tongue	32	13	2.5[b]	72	31	2.3[b]	50	18	2.7[b]	29	18	1.6[b]	183	81	2.3[b]
Salivary gland	11	4	2.5[b]	21	11	1.9[b]	5	7	0.7	15	8	1.9[b]	52	31	1.7[b]
Gum, other mouth	34	19	1.8[b]	90	47	1.9[b]	46	28	1.7[b]	43	29	1.5[b]	213	122	1.7[b]
Pharynx	25	15	1.6[b]	66	38	1.7[b]	38	22	1.7[b]	38	21	1.8[b]	167	97	1.7[b]
Digestive system	**599**	**560**	**1.1**	**1,718**	**1,458**	**1.2**[b]	**1,103**	**920**	**1.2**[b]	**1,448**	**1,064**	**1.4**[b]	**4,868**	**4,000**	**1.2**[b]
Esophagus	43	27	1.6[b]	94	66	1.4[b]	64	39	1.7[b]	49	38	1.3	250	169	1.5[b]
Stomach	79	92	0.9	230	230	1.0	144	138	1.0	150	144	1.0	603	603	1.0
Small intestine	9	5	1.9	31	12	2.6[b]	15	8	2.0[b]	13	9	1.5	68	33	2.1[b]
Colon	253	230	1.1	740	613	1.2[b]	541	397	1.4[b]	748	484	1.5[b]	2,282	1,724	1.3[b]
Rectum	101	112	0.9	356	290	1.2[b]	192	182	1.1	281	206	1.4[b]	930	789	1.2[b]
Liver	16	12	1.3	38	30	1.3	20	18	1.1	19	19	1.0	93	79	1.2
Gallbladder, other biliary	15	20	0.7	50	55	0.9	29	36	0.8	50	45	1.1	144	157	0.9
Pancreas	74	56	1.3[b]	160	147	1.1	88	93	0.9	122	110	1.1	444	407	1.1
Respiratory system	**219**	**250**	**0.9**[b]	**843**	**631**	**1.3**[b]	**574**	**374**	**1.5**[b]	**581**	**381**	**1.5**[b]	**2,217**	**1,635**	**1.4**[b]
Nasal cavities, sinuses	6	4	1.7	17	9	1.9[b]	6	6	1.1	7	6	1.2	36	24	1.5[b]
Larynx	27	25	1.1	78	61	1.3[b]	57	35	1.6[b]	41	32	1.3	203	153	1.3[b]
Trachea, bronchus, lung	182	219	0.8[b]	745	555	1.3[b]	509	330	1.5[b]	529	340	1.6[b]	1,965	1,442	1.4[b]
Other respiratory	4	1	5.3[b]	3	2	1.6	1	1	0.9	4	1	3.6	12	5	2.5[b]
Breast	374	196	1.9[b]	1,170	570	2.1[b]	728	400	1.8[b]	862	528	1.6[b]	3,134	1,693	1.9[b]
Female genital tract	**188**	**124**	**1.5**[b]	**379**	**356**	**1.1**	**287**	**246**	**1.2**[b]	**362**	**309**	**1.2**[b]	**1,216**	**1,034**	**1.2**[b]
Cervix uteri	29	26	1.1	57	72	0.8	42	47	0.9	34	51	0.7[b]	162	195	0.8[b]
Corpus uteri	52	49	1.1	144	143	1.0	122	102	1.2	150	136	1.1	468	429	1.1
Uterus, NOS	8	9	0.9	18	25	0.7	9	16	0.6	25	16	1.6[b]	60	66	0.9
Ovary, fallopian tubes	88	33	2.6[b]	132	97	1.4[b]	87	67	1.3[b]	116	86	1.3[b]	423	284	1.5[b]
Prostate gland	295	198	1.5[b]	451	497	0.9[b]	245	288	0.8[b]	290	268	1.1	1,281	1,250	1.0
Testis	5	2	3.0	7	4	1.8	5	2	2.4	2	2	1.2	19	9	2.0[b]
Kidney, renal pelvis, ureter	99	37	2.7[b]	153	94	1.6[b]	78	58	1.3[b]	102	64	1.6[b]	432	253	1.7[b]
Bladder, other urinary	118	96	1.2[b]	346	246	1.4[b]	135	150	0.9	208	161	1.3[b]	807	653	1.2[b]
Melanoma of the skin	42	20	2.1[b]	71	52	1.4[b]	44	33	1.3	48	36	1.3	205	141	1.5[b]
Eye	5	3	1.8	12	7	1.7	3	4	0.7	8	5	1.6	28	19	1.5
Brain, central nervous system	16	18	0.9	42	46	0.9	29	28	1.0	35	31	1.1	122	123	1.0
Thyroid gland	25	8	3.1[b]	25	22	1.1	24	14	1.7[b]	29	17	1.8[b]	103	61	1.7[b]
Endocrine gland	4	1	4.5[b]	8	2	3.5[b]	0	1	0.0	1	1	0.7	13	6	2.2[b]
Bone	4	3	1.5	13	7	1.9[b]	5	4	1.3	8	4	2.0	30	17	1.7[b]
Connective tissue	16	8	1.9[b]	42	22	2.0[b]	30	13	2.3[b]	28	15	1.9[b]	116	58	2.0[b]
Lymphatic, hematopoietic system	**94**	**115**	**0.8**	**317**	**304**	**1.0**	**235**	**194**	**1.2**[b]	**279**	**231**	**1.2**[b]	**925**	**843**	**1.1**[b]
Non-Hodgkin's lymphoma	36	39	0.9	96	105	0.9	69	67	1.0	96	81	1.2	297	291	1.0
Hodgkin's disease	5	8	0.6	14	21	0.7	12	13	0.9	15	14	1.1	46	56	0.8
Multiple myeloma	15	18	0.8	48	49	1.0	34	32	1.1	43	41	1.1	140	140	1.0
Leukemias	38	49	0.8	159	128	1.2[b]	120	81	1.5[b]	125	96	1.3[b]	442	354	1.2[b]
Chronic lymphocytic	10	15	0.7	32	39	0.8	29	25	1.2	34	30	1.1	105	110	1.0
Acute nonlymphocytic	19	15	1.3	73	40	1.8[b]	52	26	2.0[b]	51	32	1.6[b]	195	113	1.7[b]

[a] ICD-O codes = 140–199.

[b] $P < .05$.

ALL CANCER SITES
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	120,253			72,491			27,260			11,826			120,253		
Person-yr in interval	74,176			171,396			90,796			73,510			409,878		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1,249**	**1,045**	**1.2**[b]	**2,963**	**2,546**	**1.2**[b]	**1,667**	**1,435**	**1.2**[b]	**1,628**	**1,273**	**1.3**[b]	**7,507**	**6,295**	**1.2**[b]
Buccal cavity, pharynx	**105**	**52**	**2.0**[b]	**214**	**121**	**1.8**[b]	**117**	**66**	**1.8**[b]	93	55	**1.7**[b]	529	293	**1.8**[b]
Lip	14	10	1.5	30	22	1.3	20	12	1.6[b]	19	10	1.9[b]	83	54	1.5[b]
Tongue	28	10	2.8[b]	52	24	2.2[b]	34	13	2.7[b]	21	10	2.0[b]	135	57	2.4[b]
Salivary gland	9	3	3.4[b]	12	7	1.8	3	4	0.8	7	3	2.1	31	16	1.9[b]
Gum, other mouth	25	14	1.7[b]	60	34	1.8[b]	24	18	1.3	22	15	1.4	131	82	1.6[b]
Pharynx	21	13	1.7[b]	51	30	1.7[b]	30	16	1.8[b]	22	14	1.6[b]	124	72	1.7[b]
Digestive system	**355**	**336**	**1.1**	922	**811**	**1.1**[b]	**522**	**454**	**1.1**[b]	**506**	**396**	**1.3**[b]	**2,305**	**1,995**	**1.2**[b]
Esophagus	31	22	1.4	74	52	1.4[b]	45	28	1.6[b]	32	23	1.4	182	125	1.5[b]
Stomach	58	62	0.9	136	146	0.9	73	80	0.9	72	66	1.1	339	353	1.0
Small intestine	6	3	2.3	16	6	2.6[b]	4	3	1.2	8	3	2.7[b]	34	15	2.3[b]
Colon	137	126	1.1	363	310	1.2[b]	226	176	1.3[b]	246	160	1.5[b]	972	771	1.3[b]
Rectum	52	69	0.8[b]	197	166	1.2[b]	95	93	1.0	79	80	1.0	423	408	1.0
Liver	11	8	1.4	27	19	1.4	13	11	1.2	11	9	1.2	62	47	1.3[b]
Gallbladder, other biliary	5	9	0.6	19	22	0.9	12	13	0.9	8	11	0.7	44	56	0.8
Pancreas	50	34	1.5[b]	82	82	1.0	52	46	1.1	46	41	1.1	230	203	1.1
Respiratory system	**172**	**206**	**0.8**[b]	**640**	499	**1.3**[b]	**418**	**278**	**1.5**[b]	339	**243**	**1.4**[b]	**1,569**	**1,225**	**1.3**[b]
Nasal cavities, sinuses	5	2	2.2	11	5	2.0[b]	2	3	0.7	3	3	1.1	21	13	1.6
Larynx	20	23	0.9	68	54	1.3	47	29	1.6[b]	26	24	1.1	161	130	1.2[b]
Trachea, bronchus, lung	144	179	0.8[b]	559	435	1.3[b]	369	243	1.5[b]	306	215	1.4[b]	1,378	1,071	1.3[b]
Other respiratory	3	1	5.8[b]	2	1	1.7	0	1	0.0	4	1	8.0[b]	9	3	3.2[b]
Breast	2	2	0.9	9	5	1.7	7	3	2.4	3	3	1.1	21	13	1.6
Prostate gland	295	198	1.5[b]	451	497	0.9[b]	245	288	0.8[b]	290	268	1.1	1,281	1,250	1.0
Testis	5	2	3.0	7	4	1.8	5	2	2.4	2	2	1.2	19	9	2.0[b]
Kidney, renal pelvis, ureter	64	25	2.5[b]	107	61	1.7[b]	40	34	1.2	49	30	1.6[b]	260	150	1.7[b]
Bladder, other urinary	88	76	1.2	255	187	1.4[b]	98	107	0.9	100	97	1.0	541	467	1.2[b]
Melanoma of the skin	20	11	1.8[b]	34	27	1.3	21	15	1.4	23	13	1.7[b]	98	66	1.5[b]
Eye	2	1	1.4	4	3	1.2	1	2	0.5	2	2	1.3	9	8	1.1
Brain, central nervous system	9	10	0.9	20	24	0.8	16	13	1.2	9	11	0.8	54	58	0.9
Thyroid gland	14	3	5.3[b]	9	6	1.4	5	3	1.5	6	3	2.1	34	15	2.2[b]
Endocrine gland	2	1	3.9	2	1	1.7	0	1	0.0	0	0	0.0	4	3	1.4
Bone	3	2	2.0	7	4	2.0	3	2	1.6	1	1	0.7	14	8	1.7
Connective tissue	13	5	2.5[b]	23	12	1.9[b]	11	7	1.6	11	6	1.8	58	31	1.9[b]
Lymphatic, hematopoietic system	**60**	**68**	**0.9**	**187**	**167**	**1.1**	**100**	**94**	**1.1**	**127**	**85**	**1.5**[b]	**474**	**414**	**1.1**[b]
Non-Hodgkin's lymphoma	22	22	1.0	51	53	1.0	27	30	0.9	44	26	1.7[b]	144	130	1.1
Hodgkin's disease	3	5	0.6	9	11	0.8	4	6	0.7	7	5	1.4	23	27	0.9
Multiple myeloma	4	10	0.4[b]	30	26	1.2	11	15	0.8	18	14	1.3	63	64	1.0
Leukemias	31	31	1.0	97	77	1.3[b]	58	44	1.3	58	40	1.4[b]	244	193	1.3[b]
Chronic lymphocytic	9	10	0.9	24	25	1.0	16	15	1.1	17	14	1.3	66	63	1.0
Acute nonlymphocytic	15	9	1.6	42	23	1.8[b]	23	13	1.7[b]	27	13	2.1[b]	107	58	1.8[b]

[a] ICD-O codes = 140–199.

[b] $P < .05$.

ALL CANCER SITES
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among females in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	133,283			96,443			47,171			25,143			133,283		
Person-yr in interval	91,708			261,725			173,072			199,341			725,846		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1,037**	**740**	**1.4^b**	**3,072**	**2,147**	**1.4^b**	**2,128**	**1,524**	**1.4^b**	**2,983**	**2,095**	**1.4^b**	**9,220**	**6,502**	**1.4^b**
Buccal cavity, pharynx	**21**	**13**	**1.6^b**	**78**	**38**	**2.1^b**	**50**	**27**	**1.9^b**	**60**	**37**	**1.6^b**	**209**	**114**	**1.8^b**
Lip	2	1	2.5	2	2	0.9	2	2	1.3	4	2	1.8	10	7	1.5
Tongue	4	3	1.5	20	8	2.6^b	16	6	2.9^b	8	8	1.1	48	23	2.1^b
Salivary gland	2	2	1.2	9	5	1.9	2	3	0.6	8	4	1.8	21	14	1.5
Gum, other mouth	9	4	2.0	30	13	2.3^b	22	9	2.3^b	21	13	1.6	82	40	2.0^b
Pharynx	4	3	1.4	15	8	1.8	8	6	1.3	16	8	2.0^b	43	25	1.7^b
Digestive system	**244**	**224**	**1.1**	**796**	**647**	**1.2^b**	**581**	**465**	**1.2^b**	**942**	**668**	**1.4^b**	**2,563**	**2,005**	**1.3^b**
Esophagus	12	5	2.4^b	20	15	1.4	19	10	1.8^b	17	15	1.2	68	45	1.5^b
Stomach	21	30	0.7	94	84	1.1	71	59	1.2	78	78	1.0	264	250	1.1
Small intestine	3	2	1.5	15	6	2.5^b	11	4	2.6^b	5	6	0.9	34	18	1.9^b
Colon	116	105	1.1	377	304	1.2^b	315	221	1.4^b	502	325	1.5^b	1,310	953	1.4^b
Rectum	49	43	1.1	159	124	1.3^b	97	89	1.1	202	126	1.6^b	507	381	1.3^b
Liver	5	4	1.3	11	11	1.0	7	7	1.0	8	10	0.8	31	32	1.0
Gallbladder, other biliary	10	11	0.9	31	33	1.0	17	24	0.7	42	34	1.2	100	101	1.0
Pancreas	24	22	1.1	78	65	1.2	36	47	0.8	76	70	1.1	214	204	1.1
Respiratory system	**47**	**45**	**1.1**	**203**	**133**	**1.5^b**	**156**	**96**	**1.6^b**	**242**	**137**	**1.8^b**	**648**	**411**	**1.6^b**
Nasal cavities, sinuses	1	1	0.8	6	4	1.7	4	3	1.6	4	3	1.2	15	11	1.4
Larynx	7	3	2.7^b	10	8	1.3	10	6	1.8	15	8	2.0^b	42	24	1.8^b
Trachea, bronchus, lung	38	40	0.9	186	120	1.6^b	140	87	1.6^b	223	125	1.8^b	587	372	1.6^b
Other respiratory	1	0	4.2	1	1	1.5	1	0	2.3	0	1	0.0	3	2	1.5
Breast	372	194	1.9^b	1,161	565	2.1^b	721	397	1.8^b	859	525	1.6^b	3,113	1,680	1.9^b
Female genital tract	**188**	**124**	**1.5^b**	**379**	**356**	**1.1**	**287**	**246**	**1.2^b**	**362**	**309**	**1.2^b**	**1,216**	**1,034**	**1.2^b**
Cervix uteri	29	26	1.1	57	72	0.8	42	47	0.9	34	51	0.7^b	162	195	0.8^b
Corpus uteri	52	49	1.1	144	143	1.0	122	102	1.2	150	136	1.1	468	429	1.1
Uterus, NOS	8	9	0.9	18	25	0.7	9	16	0.6	25	16	1.6^b	60	66	0.9
Ovary, fallopian tubes	88	33	2.6^b	132	97	1.4^b	87	67	1.3^b	116	86	1.3^b	423	284	1.5^b
Kidney, renal pelvis, ureter	35	11	3.1^b	46	33	1.4^b	38	24	1.6^b	53	34	1.6^b	172	102	1.7^b
Bladder, other urinary	30	20	1.5^b	91	59	1.5^b	37	43	0.9	108	64	1.7^b	266	186	1.4^b
Melanoma of the skin	22	9	2.5^b	37	26	1.4^b	23	18	1.3	25	23	1.1	107	75	1.4^b
Eye	3	1	2.4	8	4	2.2	2	3	0.8	6	3	1.8	19	11	1.8^b
Brain, central nervous system	7	7	0.9	22	22	1.0	13	15	0.8	26	20	1.3	68	65	1.0
Thyroid gland	11	5	2.0^b	16	16	1.0	19	11	1.7^b	23	14	1.7^b	69	46	1.5^b
Endocrine gland	2	0	5.2	6	1	5.4^b	0	1	0.0	1	1	1.1	9	3	2.9^b
Bone	1	1	0.9	6	3	1.9	2	2	0.9	7	3	2.8^b	16	9	1.8^b
Connective tissue	3	3	0.9	19	9	2.1^b	19	6	3.0^b	17	8	2.0^b	58	27	2.1^b
Lymphatic, hematopoietic system	**34**	**47**	**0.7**	**130**	**137**	**0.9**	**135**	**99**	**1.4^b**	**152**	**146**	**1.0**	**451**	**428**	**1.1**
Non-Hodgkin's lymphoma	14	18	0.8	45	52	0.9	42	38	1.1	52	54	1.0	153	161	0.9
Hodgkin's disease	2	3	0.6	5	10	0.5	8	7	1.2	8	9	0.9	23	29	0.8
Multiple myeloma	11	8	1.4	18	24	0.8	23	17	1.3	25	27	0.9	77	76	1.0
Leukemias	7	18	0.4^b	62	51	1.2	62	37	1.7^b	67	55	1.2	198	161	1.2^b
Chronic lymphocytic	1	5	0.2	8	14	0.6	13	11	1.2	17	17	1.0	39	46	0.8
Acute nonlymphocytic	4	6	0.7	31	17	1.8^b	29	13	2.3^b	24	19	1.3	88	55	1.6^b

[a] ICD-O codes = 140–199.

[b] $P < .05$.

ALL CANCER SITES
BOTH SEXES
LONG-TERM SURVIVORS

TABLE 1F.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males and females, long-term survivors in Connecticut, 1935-82*[a]

	Yr after first primary cancer diagnosis														
	1-9 yr			10-19 yr			20-29 yr			30+ yr			Total (<1-30+ yr)		
No. starting interval	168,934			36,969			10,297			2,218			253,536		
Person-yr in interval	696,989			208,178			54,374			10,298			1,135,724		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**9,830**	**7,649**	**1.3^b**	**3,297**	**2,488**	**1.3^b**	**1,086**	**725**	**1.5^b**	**228**	**157**	**1.5^b**	**16,727**	**12,797**	**1.3^b**
Buccal cavity, pharynx	**459**	**252**	**1.8^b**	**119**	**70**	**1.7^b**	**31**	**18**	**1.8^b**	**3**	**3**	**0.9**	**738**	**407**	**1.8^b**
Lip	54	38	1.4^b	21	10	2.2^b	2	2	1.0	0	0	0.0	93	61	1.5^b
Tongue	122	50	2.5^b	22	14	1.6	6	3	1.7	1	1	1.6	183	81	2.3^b
Salivary gland	26	18	1.4	13	6	2.2^b	2	2	1.2	0	0	0.0	52	31	1.7^b
Gum, other mouth	136	75	1.8^b	29	22	1.3	14	6	2.4^b	0	1	0.0	213	122	1.7^b
Pharynx	104	60	1.7^b	31	17	1.9^b	5	4	1.2	2	1	2.8	167	97	1.7^b
Digestive system	**2,821**	**2,377**	**1.2^b**	**1,008**	**780**	**1.3^b**	**367**	**232**	**1.6^b**	**73**	**53**	**1.4^b**	**4,868**	**4,000**	**1.2^b**
Esophagus	158	105	1.5^b	37	29	1.3	7	7	1.0	5	1	3.4^b	250	169	1.5^b
Stomach	374	368	1.0	105	109	1.0	41	29	1.4^b	4	6	0.7	603	603	1.0
Small intestine	46	20	2.3^b	10	6	1.6	3	2	1.6	0	0	0.0	68	33	2.1^b
Colon	1,281	1,010	1.3^b	520	349	1.5^b	196	110	1.8^b	32	26	1.2	2,282	1,724	1.3^b
Rectum	548	472	1.2^b	193	152	1.3^b	69	44	1.6^b	19	10	1.9^b	930	789	1.2^b
Liver	58	48	1.2	13	14	0.9	4	4	1.0	2	1	2.3	93	79	1.2
Gallbladder, other biliary	79	91	0.9	35	33	1.1	15	10	1.5	0	2	0.0	144	157	0.9
Pancreas	248	240	1.0	84	80	1.0	29	25	1.2	9	6	1.6	444	407	1.1
Respiratory system	**1,417**	**1,005**	**1.4^b**	**441**	**289**	**1.5^b**	**117**	**77**	**1.5^b**	**23**	**15**	**1.5**	**2,217**	**1,635**	**1.4^b**
Nasal cavities, sinuses	23	15	1.6^b	7	4	1.6	0	1	0.0	0	0	0.0	36	24	1.5^b
Larynx	135	96	1.4^b	32	25	1.3	9	6	1.6	0	1	0.0	203	153	1.3^b
Trachea, bronchus, lung	1,254	884	1.4^b	399	257	1.6^b	107	69	1.5^b	23	14	1.7^b	1,965	1,442	1.4^b
Other respiratory	4	3	1.4	3	1	3.6	1	0	4.3	0	0	0.0	12	5	2.5^b
Breast	1,898	970	2.0^b	616	376	1.6^b	203	124	1.6^b	43	29	1.5^b	3,134	1,693	1.9^b
Female genital tract	**666**	**602**	**1.1^b**	**256**	**226**	**1.1^b**	**87**	**69**	**1.3^b**	**19**	**14**	**1.3**	**1,216**	**1,034**	**1.2^b**
Cervix uteri	99	118	0.8	27	39	0.7	7	10	0.7	0	2	0.0	162	195	0.8^b
Corpus uteri	266	245	1.1	101	98	1.0	41	32	1.3	8	7	1.2	468	429	1.1
Uterus, NOS	27	41	0.7^b	19	12	1.5	6	3	2.1	0	1	0.0	60	66	0.9
Ovary, fallopian tubes	219	164	1.3^b	78	62	1.2	28	19	1.4	10	4	2.4^b	423	284	1.5^b
Prostate gland	696	785	0.9^b	227	213	1.1	54	48	1.1	9	7	1.2	1,281	1,250	1.0
Testis	12	6	2.0^b	1	1	0.7	1	0	3.4	0	0	0.0	19	9	2.0^b
Kidney, renal pelvis, ureter	231	152	1.5^b	62	47	1.3^b	35	13	2.6^b	5	3	1.8	432	253	1.7^b
Bladder, other urinary	481	396	1.2^b	147	121	1.2^b	41	33	1.2	20	7	2.8^b	807	653	1.2^b
Melanoma of the skin	115	85	1.4^b	30	27	1.1	15	8	1.9^b	3	2	1.8	205	141	1.5^b
Eye	15	11	1.3	4	4	1.1	4	1	3.8^b	0	0	0.0	28	19	1.5
Brain, central nervous system	71	74	1.0	29	23	1.3	5	7	0.8	1	1	0.8	122	123	1.0
Thyroid gland	49	37	1.3	23	12	1.9^b	5	4	1.4	1	1	1.4	103	61	1.7^b
Endocrine gland	8	4	2.2	1	1	0.9	0	0	0.0	0	0	0.0	13	6	2.2^b
Bone	18	11	1.7^b	6	3	2.0	1	1	1.3	1	0	6.3	30	17	1.7^b
Connective tissue	72	35	2.1^b	19	11	1.7^b	7	3	2.3	2	1	3.2	116	58	2.0^b
Lymphatic, hematopoietic system	**552**	**497**	**1.1^b**	**200**	**168**	**1.2^b**	**63**	**52**	**1.2**	**16**	**12**	**1.3**	**925**	**843**	**1.1^b**
Non-Hodgkin's lymphoma	165	172	1.0	73	58	1.3	21	18	1.2	2	4	0.5	297	291	1.0
Hodgkin's disease	26	34	0.8	11	11	1.0	3	3	1.0	1	1	2.0	46	56	0.8
Multiple myeloma	82	81	1.0	28	29	1.0	8	10	0.8	7	2	3.0^b	140	140	1.0
Leukemias	279	210	1.3^b	88	70	1.3^b	31	21	1.5	6	5	1.2	442	354	1.2^b
Chronic lymphocytic	61	65	0.9	22	22	1.0	10	7	1.5	2	2	1.3	105	110	1.0
Acute nonlymphocytic	125	66	1.9^b	32	23	1.4	18	7	2.5^b	1	2	0.6	195	113	1.7^b

[a] ICD-O codes = 140-199.
[b] $P < .05$.

ALL CANCER SITES
MALES
LONG-TERM SURVIVORS

TABLE 1G.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	72,491			11,826			2,500			407			120,253		
Person-yr in interval	262,192			59,705			11,988			1,817			409,878		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4,630**	**3,980**	**1.2[b]**	**1,259**	**1,018**	**1.2[b]**	**326**	**221**	**1.5[b]**	**43**	**34**	**1.3**	**7,507**	**6,295**	**1.2[b]**
Buccal cavity, pharynx	**331**	**187**	**1.8[b]**	**73**	**44**	**1.6[b]**	**19**	**9**	**2.1[b]**	**1**	**1**	**0.8**	**529**	**293**	**1.8[b]**
Lip	50	35	1.4[b]	18	8	2.2[b]	1	2	0.7	0	0	0.0	83	54	1.5[b]
Tongue	86	37	2.4[b]	15	9	1.8	6	2	3.6[b]	0	0	0.0	135	57	2.4[b]
Salivary gland	15	10	1.5	6	3	2.3	1	1	1.8	0	0	0.0	31	16	1.9[b]
Gum, other mouth	84	52	1.6[b]	14	12	1.1	8	3	3.2[b]	0	0	0.0	131	82	1.6[b]
Pharynx	81	46	1.8[b]	18	11	1.6	3	2	1.3	1	0	3.0	124	72	1.7[b]
Digestive system	**1,444**	**1,265**	**1.1[b]**	**394**	**318**	**1.2[b]**	**100**	**68**	**1.5[b]**	**12**	**10**	**1.2**	**2,305**	**1,995**	**1.2[b]**
Esophagus	119	80	1.5[b]	27	19	1.4	4	4	1.1	1	1	1.9	182	125	1.5[b]
Stomach	209	225	0.9	53	54	1.0	16	11	1.5	3	1	2.0	339	353	1.0
Small intestine	20	10	2.1[b]	7	2	3.0[b]	1	1	2.0	0	0	0.0	34	15	2.3[b]
Colon	589	486	1.2[b]	183	127	1.4[b]	56	28	2.0[b]	7	4	1.6	972	771	1.3[b]
Rectum	292	259	1.1[b]	68	64	1.1	11	14	0.8	0	2	0.0	423	408	1.0
Liver	40	30	1.3	8	7	1.1	3	2	1.9	0	0	0.0	62	47	1.3[b]
Gallbladder, other biliary	31	35	0.9	7	9	0.8	1	2	0.5	0	0	0.0	44	56	0.8
Pancreas	134	129	1.0	38	33	1.2	8	7	1.2	0	1	0.0	230	203	1.1
Respiratory system	**1,058**	**776**	**1.4[b]**	**266**	**194**	**1.4[b]**	**61**	**42**	**1.4[b]**	**12**	**7**	**1.8**	**1,569**	**1,225**	**1.3[b]**
Nasal cavities, sinuses	13	8	1.5	3	2	1.4	0	0	0.0	0	0	0.0	21	13	1.6
Larynx	115	83	1.4[b]	20	20	1.0	6	4	1.5	0	1	0.0	161	130	1.2[b]
Trachea, bronchus, lung	928	678	1.4[b]	240	171	1.4[b]	54	38	1.4[b]	12	6	2.0[b]	1,378	1,071	1.3[b]
Other respiratory	2	2	1.1	3	0	7.3[b]	1	0	12.7	0	0	0.0	9	3	3.2[b]
Breast	16	8	1.9[b]	2	2	1.0	1	0	2.1	0	0	0.0	21	13	1.6
Prostate gland	696	785	0.9[b]	227	213	1.1	54	48	1.1	9	7	1.2	1,281	1,250	1.0
Testis	12	6	2.0[b]	1	1	0.7	1	0	3.4	0	0	0.0	19	9	2.0[b]
Kidney, renal pelvis, ureter	147	95	1.5[b]	33	24	1.4	15	5	2.9[b]	1	1	1.3	260	150	1.7[b]
Bladder, other urinary	353	294	1.2[b]	74	77	1.0	22	17	1.3	4	3	1.5	541	467	1.2[b]
Melanoma of the skin	55	41	1.3[b]	16	10	1.5	6	2	2.5	1	0	2.4	98	66	1.5[b]
Eye	5	5	0.9	1	1	0.8	1	0	4.0	0	0	0.0	9	8	1.1
Brain, central nervous system	36	37	1.0	9	9	1.0	0	2	0.0	0	0	0.0	54	58	0.9
Thyroid gland	14	10	1.4	6	2	2.6	0	0	0.0	0	0	0.0	34	15	2.2[b]
Endocrine gland	2	2	1.1	0	0	0.0	0	0	0.0	0	0	0.0	4	3	1.4
Bone	10	5	1.9	1	1	0.8	0	0	0.0	0	0	0.0	14	8	1.7
Connective tissue	34	19	1.8[b]	10	5	2.0	1	1	0.9	0	0	0.0	58	31	1.9[b]
Lymphatic, hematopoietic system	**287**	**261**	**1.1**	**102**	**68**	**1.5[b]**	**22**	**15**	**1.5**	**3**	**2**	**1.3**	**474**	**414**	**1.1[b]**
Non-Hodgkin's lymphoma	78	82	0.9	36	21	1.7[b]	7	5	1.5	1	1	1.3	144	130	1.1
Hodgkin's disease	13	17	0.8	4	4	1.0	2	1	2.4	1	0	8.4	23	27	0.9
Multiple myeloma	41	40	1.0	16	11	1.5	1	2	0.4	1	0	2.6	63	64	1.0
Leukemias	155	121	1.3[b]	46	32	1.4[b]	12	7	1.7	0	1	0.0	244	193	1.3[b]
Chronic lymphocytic	40	40	1.0	14	11	1.3	3	2	1.2	0	0	0.0	66	63	1.0
Acute nonlymphocytic	65	36	1.8[b]	19	10	1.9[b]	8	2	3.4[b]	0	0	0.0	107	58	1.8[b]

[a] ICD-O codes = 140–199.

[b] $P < .05$.

ALL CANCER SITES
FEMALES
LONG-TERM SURVIVORS

TABLE 1H.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among females, long-term survivors in Connecticut, 1935–82*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval Person-yr in interval	96,443 434,797			25,143 148,473			7,797 42,386			1,811 8,481			133,283 725,846		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**5,200**	**3,670**	**1.4^b**	**2,038**	**1,470**	**1.4^b**	**760**	**504**	**1.5^b**	**185**	**122**	**1.5^b**	**9,220**	**6,502**	**1.4^b**
Buccal cavity, pharynx	**128**	**65**	**2.0^b**	**46**	**26**	**1.8^b**	**12**	**9**	**1.4**	**2**	**2**	**1.0**	**209**	**114**	**1.8^b**
Lip	4	4	1.0	3	2	1.9	1	1	1.9	0	0	0.0	10	7	1.5
Tongue	36	13	2.7^b	7	5	1.3	0	2	0.0	1	0	2.5	48	23	2.1^b
Salivary gland	11	8	1.3	7	3	2.2	1	1	0.9	0	0	0.0	21	14	1.5
Gum, other mouth	52	23	2.3^b	15	9	1.6	6	3	1.9	0	1	0.0	82	40	2.0^b
Pharynx	23	14	1.6^b	13	6	2.3^b	2	2	1.1	1	0	2.7	43	25	1.7^b
Digestive system	**1,377**	**1,112**	**1.2^b**	**614**	**461**	**1.3^b**	**267**	**165**	**1.6^b**	**61**	**43**	**1.4^b**	**2,563**	**2,005**	**1.3^b**
Esophagus	39	25	1.5^b	10	10	1.0	3	4	0.8	4	1	4.4^b	68	45	1.5^b
Stomach	165	143	1.2	52	55	0.9	25	18	1.4	1	4	0.2	264	250	1.1
Small intestine	26	10	2.6^b	3	4	0.7	2	1	1.5	0	0	0.0	34	18	1.9^b
Colon	692	524	1.3^b	337	222	1.5^b	140	81	1.7^b	25	22	1.2	1,310	953	1.4^b
Rectum	256	213	1.2^b	125	87	1.4^b	58	31	1.9^b	19	8	2.5^b	507	381	1.3^b
Liver	18	18	1.0	5	7	0.7	1	2	0.4	2	1	3.3	31	32	1.0
Gallbladder, other biliary	48	56	0.9	28	23	1.2	14	8	1.7	0	2	0.0	100	101	1.0
Pancreas	114	112	1.0	46	48	1.0	21	18	1.2	9	5	1.9	214	204	1.1
Respiratory system	**359**	**229**	**1.6^b**	**175**	**94**	**1.9^b**	**56**	**35**	**1.6^b**	**11**	**8**	**1.3**	**648**	**411**	**1.6^b**
Nasal cavities, sinuses	10	6	1.6	4	2	1.7	0	1	0.0	0	0	0.0	15	11	1.4
Larynx	20	13	1.5	12	5	2.2^b	3	2	1.7	0	0	0.0	42	24	1.8^b
Trachea, bronchus, lung	326	206	1.6^b	159	86	1.9^b	53	32	1.7^b	11	8	1.4	587	372	1.6^b
Other respiratory	2	1	1.8	0	0	0.0	0	0	0.0	0	0	0.0	3	2	1.5
Breast	1,882	961	2.0^b	614	373	1.6^b	202	123	1.6^b	43	29	1.5^b	3,113	1,680	1.9^b
Female genital tract	**666**	**602**	**1.1^b**	**256**	**226**	**1.1^b**	**87**	**69**	**1.3^b**	**19**	**14**	**1.3**	**1,216**	**1,034**	**1.2^b**
Cervix uteri	99	118	0.8	27	39	0.7	7	10	0.7	0	2	0.0	162	195	0.8^b
Corpus uteri	266	245	1.1	101	98	1.0	41	32	1.3	8	7	1.2	468	429	1.1
Uterus, NOS	27	41	0.7^b	19	12	1.5	6	3	2.1	0	1	0.0	60	66	0.9
Ovary, fallopian tubes	219	164	1.3^b	78	62	1.2	28	19	1.4	10	4	2.4^b	423	284	1.5^b
Kidney, renal pelvis, ureter	84	57	1.5^b	29	24	1.2	20	8	2.4^b	4	2	2.0	172	102	1.7^b
Bladder, other urinary	128	102	1.3^b	73	44	1.7^b	19	16	1.2	16	4	3.6^b	266	186	1.4^b
Melanoma of the skin	60	43	1.4^b	14	16	0.8	9	5	1.6	2	1	1.6	107	75	1.4^b
Eye	10	6	1.6	3	2	1.2	3	1	3.7	0	0	0.0	19	11	1.8^b
Brain, central nervous system	35	37	0.9	20	15	1.4	5	5	1.1	1	1	1.0	68	65	1.0
Thyroid gland	35	27	1.3	17	10	1.7	5	3	1.6	1	1	1.6	69	46	1.5^b
Endocrine gland	6	2	3.2^b	1	1	1.5	0	0	0.0	0	0	0.0	9	3	2.9^b
Bone	8	5	1.5	5	2	2.7	1	1	1.8	1	0	8.1	16	9	1.8^b
Connective tissue	38	16	2.4^b	9	6	1.5	6	2	3.1^b	2	0	4.3	58	27	2.1^b
Lymphatic, hematopoietic system	**265**	**236**	**1.1**	**98**	**100**	**1.0**	**41**	**37**	**1.1**	**13**	**10**	**1.4**	**451**	**428**	**1.1**
Non-Hodgkin's lymphoma	87	89	1.0	37	37	1.0	14	14	1.0	1	4	0.3	153	161	0.9
Hodgkin's disease	13	17	0.8	7	6	1.1	1	2	0.5	0	0	0.0	23	29	0.8
Multiple myeloma	41	41	1.0	12	18	0.7	7	7	1.0	6	2	3.1^b	77	76	1.0
Leukemias	124	88	1.4^b	42	38	1.1	19	14	1.4	6	4	1.6	198	161	1.2^b
Chronic lymphocytic	21	25	0.8	8	11	0.7	7	4	1.6	2	1	1.7	39	46	0.8
Acute nonlymphocytic	60	30	2.0^b	13	13	1.0	10	5	2.0	1	1	0.7	88	55	1.6^b

[a] ICD-O codes = 140–199.

[b] $P < .05$.

ALL CANCER SITES
EXCLUDING SAME SITE
BOTH SEXES

TABLE 2A. *Observed (O) and expected (E) numbers of second primary cancers after diagnosis of any first primary cancer, excluding initial cancers of the same site among males and females in Connecticut, 1935–82*[a]

Second primary cancer site	Total			10+ yr survivors		
	O	E	O/E	O	E	O/E
All second cancers	**12,831**	**10,428**	**1.2**[b]	**3,604**	**2,731**	**1.3**[b]
Buccal cavity, pharynx	**574**	**390**	**1.5**[b]	**122**	**86**	**1.4**[b]
Lip	71	56	1.3	18	11	1.7[b]
Tongue	129	76	1.7[b]	20	17	1.2
Salivary gland	52	30	1.7[b]	15	8	1.9[b]
Gum, other mouth	136	115	1.2	27	27	1.0
Pharynx	156	96	1.6[b]	37	21	1.7[b]
Digestive system	**3,910**	**3,440**	**1.1**[b]	**1,160**	**918**	**1.3**[b]
Esophagus	249	169	1.5[b]	49	38	1.3
Stomach	601	588	1.0	150	140	1.1
Small intestine	67	33	2.0[b]	13	9	1.5
Colon	1,554	1,351	1.2[b]	514	384	1.3[b]
Rectum	705	620	1.1[b]	227	163	1.4[b]
Liver	93	79	1.2	19	19	1.0[b]
Gallbladder, other bilary	142	156	0.9	50	45	1.1
Pancreas	444	405	1.1	122	110	1.1
Respiratory system	**2,105**	**1,554**	**1.4**[b]	**562**	**372**	**1.5**[b]
Nasal cavities, sinuses	36	24	1.5[b]	7	6	1.2
Larynx	201	146	1.4[b]	41	30	1.4
Trachea, bronchus, lung	1,855	1,368	1.4[b]	510	332	1.5[b]
Other respiratory	12	5	2.5[b]	4	1	3.6
Breast	1,206	1,056	1.1[b]	397	339	1.2[b]
Female genital tract	**979**	**747**	**1.3**[b]	**273**	**199**	**1.4**[b]
Cervix uteri	141	138	1.0	29	32	0.9
Corpus uteri	400	311	1.3[b]	119	88	1.4[b]
Uterus, NOS	47	47	1.0	20	10	2.0[b]
Ovary, fallopian tubes	338	205	1.6[b]	91	56	1.6[b]
Prostate gland	1,280	892	1.4[b]	290	225	1.3[b]
Testis	13	9	1.5	1	2	0.6
Kidney, renal pelvis, ureter	320	226	1.4[b]	81	58	1.4[b]
Bladder, other urinary	686	576	1.2[b]	197	144	1.4[b]
Melanoma of the skin	175	137	1.3[b]	41	36	1.2
Eye	26	19	1.4	8	5	1.6
Brain, central nervous system	120	122	1.0	34	31	1.1
Thyroid gland	98	60	1.6[b]	29	16	1.8[b]
Endocrine gland	13	6	2.2[b]	1	1	0.7
Bone	29	17	1.7[b]	8	4	2.0
Connective tissue	112	57	2.0[b]	26	14	1.8[b]
Lymphatic, hematopoietic system	**906**	**812**	**1.1**[b]	**273**	**226**	**1.2**[b]
Non-Hodgkin's lymphoma	286	279	1.0	91	78	1.2
Hodgkin's disease	45	53	0.8	15	13	1.1
Multiple myeloma	140	139	1.0	43	41	1.1
Leukemias	435	340	1.3[b]	124	93	1.3[b]
Chronic lymphocytic	105	105	1.0	34	29	1.2
Acute nonlymphocytic	189	108	1.7[b]	51	31	1.6[b]

[a] The risks were calculated for second cancers of the lip, tongue, and gum/mouth excluding patients with initial cancers of the lip, tongue, and gum/mouth; second colon and rectal cancers excluding initial colorectal cancers; second female genital cancers excluding initial female genital cancers; second urinary cancers excluding initial urinary cancers; and for second NHL, Hodgkin's disease, and leukemia excluding initial lymphomas and leukemias.

[b] $P<.05$.

ALL CANCER SITES EXCLUDING SAME SITE MALES

TABLE 2B.—*Observed (O) and expected (E) numbers of second primary cancers after diagnosis of any first primary cancer, excluding initial cancers of the same site among males in Connecticut, 1935–82*[a]

Second primary cancer site	Total			10+ yr survivors		
	O	E	O/E	O	E	O/E
All second cancers	**6,570**	**5,431**	**1.2**[b]	**1,419**	**1,123**	**1.3**[b]
Buccal cavity, pharynx	**402**	**276**	**1.5**[b]	**67**	**50**	**1.3**[b]
Lip	61	49	1.2	14	8	1.7
Tongue	91	53	1.7[b]	13	9	1.4
Salivary gland	31	16	1.9[b]	7	3	2.1
Gum, other mouth	79	76	1.0	9	14	0.7
Pharynx	115	71	1.6[b]	22	13	1.6[b]
Digestive system	**1,799**	**1,702**	**1.1**[b]	**373**	**327**	**1.1**[b]
Esophagus	182	124	1.5[b]	32	23	1.4
Stomach	337	342	1.0	72	64	1.1
Small intestine	33	15	2.2[b]	8	3	2.7[b]
Colon	599	587	1.0	136	115	1.2[b]
Rectum	294	312	0.9	56	58	1.0
Liver	62	47	1.3[b]	11	9	1.2
Gallbladder, other biliary	42	55	0.8	8	11	0.7
Pancreas	230	202	1.1	46	41	1.1
Respiratory system	**1,483**	**1,150**	**1.3**[b]	**323**	**235**	**1.4**[b]
Nasal cavities, sinuses	21	13	1.6	3	3	1.2
Larynx	159	123	1.3[b]	26	23	1.2
Trachea, bronchus, lung	1,294	1,003	1.3[b]	290	208	1.4[b]
Other respiratory	9	3	3.2[b]	4	1	8.0[b]
Breast	20	13	1.5	3	3	1.1
Prostate gland	1,280	892	1.4[b]	290	225	1.3[b]
Testis	13	9	1.5	1	2	0.6
Kidney, renal pelvis, ureter	181	128	1.4[b]	33	25	1.3
Bladder, other urinary	448	398	1.1[b]	91	82	1.1
Melanoma of the skin	84	64	1.3[b]	19	13	1.5
Eye	7	8	0.8	2	2	1.3
Brain, central nervous system	53	57	0.9	9	11	0.8
Thyroid gland	33	15	2.2[b]	6	3	2.1
Endocrine gland	4	3	1.4	0	0	0.0
Bone	13	8	1.6	1	1	0.7
Connective tissue	56	30	1.9[b]	10	6	1.7
Lymphatic, hematopoietic system	**462**	**396**	**1.2**[b]	**124**	**82**	**1.5**[b]
Non-Hodgkin's lymphoma	137	123	1.1	42	25	1.7[b]
Hodgkin's disease	23	25	0.9	7	5	1.5
Multiple myeloma	63	64	1.0	18	14	1.3
Leukemias	239	184	1.3[b]	57	39	1.5[b]
Chronic lymphocytic	66	60	1.1	17	13	1.3
Acute nonlymphocytic	103	55	1.9[b]	27	12	2.2[b]

[a] *See* footnote *a* of table 2A.

[b] $P<.05$.

ALL CANCER SITES EXCLUDING SAME SITE FEMALES

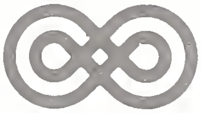
TABLE 2C. —*Observed (O) and expected (E) numbers of second primary cancers after diagnosis of any first primary cancer, excluding initial cancers of the same site among females in Connecticut, 1935–82*[a]

Second primary cancer site	Total			10+ yr survivors		
	O	E	O/E	O	E	O/E
All second cancers	**6,261**	**4,998**	**1.3**[b]	**2,185**	**1,608**	**1.4**[b]
Buccal cavity, pharynx	**172**	**113**	**1.5**[b]	**55**	**36**	**1.5**[b]
Lip	10	7	1.5	4	2	1.8
Tongue	38	23	1.6[b]	7	7	0.9
Salivary gland	21	14	1.5	8	4	1.8
Gum, other mouth	57	40	1.4[b]	18	13	1.4
Pharynx	41	25	1.6[b]	15	8	1.9[b]
Digestive system	**2,111**	**1,737**	**1.2**[b]	**787**	**590**	**1.3**[b]
Esophagus	67	45	1.5[b]	17	15	1.2
Stomach	264	246	1.1	78	77	1.0
Small intestine	34	18	1.9[b]	5	6	0.9
Colon	955	763	1.3[b]	378	269	1.4[b]
Rectum	411	309	1.3[b]	171	105	1.6[b]
Liver	31	32	1.0	8	10	0.8
Gallbladder, other biliary	100	101	1.0	42	34	1.3
Pancreas	214	203	1.1	76	70	1.1
Respiratory system	**622**	**404**	**1.5**[b]	**239**	**137**	**1.7**[b]
Nasal cavities, sinuses	15	11	1.4	4	3	1.2
Larynx	42	23	1.8[b]	15	8	2.0[b]
Trachea, bronchus, lung	561	365	1.5[b]	220	124	1.8[b]
Other respiratory	3	2	1.5	0	1	0.0
Breast	1,186	1,043	1.1[b]	394	337	1.2[b]
Female genital tract	**979**	**747**	**1.3**[b]	**273**	**199**	**1.4**[b]
Cervix uteri	141	138	1.0	29	32	0.9
Corpus uteri	400	311	1.3[b]	119	88	1.4[b]
Uterus, NOS	47	47	1.0	20	10	2.0[b]
Ovary, fallopian tubes	338	205	1.6[b]	91	56	1.6[b]
Kidney, renal pelvis, ureter	139	98	1.4[b]	48	33	1.5[b]
Bladder, other urinary	238	178	1.3[b]	106	62	1.7[b]
Melanoma of the skin	91	73	1.2	22	23	1.0
Eye	19	11	1.8[b]	6	3	1.8
Brain, central nervous system	67	65	1.0	25	20	1.2
Thyroid gland	65	45	1.4[b]	23	13	1.7[b]
Endocrine gland	9	3	2.9[b]	1	1	1.1
Bone	16	9	1.8[b]	7	3	2.8[b]
Connective tissue	56	27	2.1[b]	16	8	1.9[b]
Lymphatic, hematopoietic system	**444**	**416**	**1.1**[b]	**149**	**144**	**1.0**
Non-Hodgkin's lymphoma	149	156	1.0	49	53	0.9
Hodgkin's disease	22	28	0.8	8	9	0.9
Multiple myeloma	77	76	1.0	25	27	0.9
Leukemias	196	156	1.3[b]	67	54	1.2
Chronic lymphocytic	39	45	0.9	17	16	1.0
Acute nonlymphocytic	86	53	1.6[b]	24	19	1.3

[a] *See* footnote *a* of table 2A.

[b] $P < .05$.

III. Multiple Primary Cancers in Denmark



Cancer Registration in Denmark and the Study of Multiple Primary Cancers, 1943–80 [1]

Ole M. Jensen, Hans H. Storm, *and* Hjalgrim S. Jensen [2]

ABSTRACT—The Danish Cancer Registry began in 1942 as the world's first program to register all cases of cancer arising in an entire nation. The Registry covers a population with free access to good medical care. Voluntary notifications are received of patients with reportable malignant and certain related diseases from hospital departments, pathology institutes, and practicing physicians. The Registry is linked annually to death certificates made available by the Danish National Board of Health to ascertain additional cancers and to learn whether patients previously reported to the registry have died. During the period 1943-77, coding of the reported diseases was done by the Registry's medical and clerical staff according to an extended version of the Seventh Revision of the International Classification of Diseases (ICD). Since 1978, information has been coded according to the ICD for Oncology. Multiple primary cancers in the same patient are entered individually into the Registry; however, before 1978 only multiple primary cancers in different organs were registered. An evaluation of the completeness and the validity of diagnoses in the Danish Cancer Registry generally confirms the high quality of its data. However, it appears that the approach taken by the Registry in accepting multiple primary cancers has been a conservative one, and the risk of a person developing second cancers of some sites will thus be underestimated.—Natl Cancer Inst Monogr 68: 245-251, 1985.

The Danish Cancer Registry was founded in May 1942 as the first nationwide program to register all cases of cancer arising in a defined population. While operating under the auspices of the Danish Cancer Society, assistance was received from the Danish National Board of Health, which provided full access to death certificate data, and from the Danish Medical Association, which urged its members to report cancer patients to the Registry on a voluntary basis. The mission of the Registry as originally outlined was to collect data on patients with cancer that would serve as a basis for 1) individual follow-up of patients, 2) reliable morbidity statistics for accurate estimations of therapeutic results, and 3) an accurate evaluation of variations in the incidence of malignant neoplasms over time, as well as by geographic location, occupation, or other factors (*1*).

It soon became clear that the main emphasis of the Registry would be cancer epidemiology rather than clinical investigations because of the limited amount of information available for each patient. The efficacy of various cancer therapies could not be clearly determined from general population statistics because of the nonrandom nature of treatment selection and underreporting of complete therapeutic histories. However, the Registry could provide base-line data on survival by computing overall population-based survival rates. For a full description of the early operations of the Registry, the reader should consult the publications of Clemmesen (*1–5*).

In 1942, retrospective collection of data from the first quarter of that year was attempted. However, the 1942 data were discarded when the final figures fell far short of those for 1943 (*2*). Incident cancers reported to the Registry since 1 January 1943 are thus available for study. Reports covering the years 1943–72 have been published by Clemmesen (*2–5*) and for the period 1973–80 by the Danish Cancer Registry (*6, 7*). During 1942–76, the major part of the operating funds for the Registry were provided by the Danish Cancer Society and a small amount from the Danish National Board of Health. With the recognition of the Registry as an integral part of the Danish medical information system, governmental financial support increased. Since 1983, the basic registration of incoming notifications and the reporting of incidence data have been funded under an agreement between the Ministry for the Interior and the Danish Cancer Society. The research activities of the Danish Cancer Registry, which consume most of its annual budget, are made possible by funds from the Danish Cancer Society and from increasing extramural support provided by other national and foreign sources.

The use of the Registry data for cancer research has increased gradually. During its first years of operation, the information was used mainly for descriptive purposes, but currently the data are being used more and more for analytical studies. Exceptional record-linkage capabilities, facilitated because of the unique population identification number provided each Danish citizen, have enhanced cancer morbidity studies of various population groups, including cancer patients. Case-control studies have also been conducted with Registry material often supplemented with information from other sources.

MEDICAL CARE, DIAGNOSIS, AND TREATMENT OF CANCER

During the years covered by cancer registration in Denmark, medical care has been provided free for all Danish citizens, which included 5,123,989 persons in 1980.

ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; ICD-O = ICD for Oncology; WHO = World Health Organization.

[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100, Copenhagen, Denmark. *Address reprint requests to* Ole M. Jensen, M.D.

The medical care system is organized into a private sector of general practitioners and specialists who provide primary health care to the population under contract with the National Health Insurance. Hospital care is provided by public hospitals operating under the authority of the counties, municipalities, or the Danish State. Medical schools are located at the Universities of Copenhagen, Aarhus, and Odense.

In 1980, there were 2.2 physicians per 1,000 inhabitants in Denmark and 5.6 beds for somatic illnesses per 1,000 inhabitants (*8*); corresponding figures for 1950 were 1.0 physician and 5.8 beds. The main cause of death is cardiovascular diseases (50%), with malignant neoplasms second (25%). The expectation of life is 71.1 years for men and 77.2 years for women.

Treatment of cancer is partially centralized. During 1943–80, radiation treatment was given first at 3 and later at 5 regional radiotherapy or oncologic centers located at Finseninstitutet (Copenhagen), Copenhagen County Hospital (Herlev), Odense Hospital, Aarhus Municipality Hospital, and Aalborg Hospital. Cancer surgery and other treatments for cancer are administered in all major general hospitals, although the tendency recently is for intensive chemotherapy to be given mainly at the radiotherapy or oncologic centers. Histopathologic diagnoses of cancer are made by pathologists operating in institutes or departments of pathology at 28 major hospitals throughout the country. The autopsy rate (40%) is high in Denmark and has been virtually unchanged for the past decades (*9*). Among cancer patients the autopsy rate is around 44% (*10*).

SOURCES OF INFORMATION

The sources of information on cancer patients have been the same since 1942. Hospital departments voluntarily notify the Registry of malignant and related diseases when a cancer is diagnosed and when changes in initial diagnosis and treatment occur. In addition, reports are received from departments of pathology and forensic medicine on the results of autopsies of cancer patients. Cancers first recognized at autopsy are also reported and are included in the Registry's material, irrespective of whether the cancer is suspected before death or is an incidental finding at autopsy. During the past decades, the Registry has also received notifications from practicing dermatologists who report large numbers of nonmelanoma skin cancers diagnosed and treated in physicians' offices.

The National Board of Health each year makes available all death certificates for cross-linkage with the Registry's material. Before a cancer appearing only on a death certificate is included in the data base, each case is thoroughly investigated by contact with the certifying hospital department or practicing physician. Cancers are not included if the diagnosis is not verified. Occasionally, information is not available from the certifying physician, and the information on the death certificates for such cases are included even if the reliability of the cancer diagnosis may be questionable. A decreasing fraction of cancer diagnoses are based on "death certificates only," e.g., 18% of all incident cancers in 1943–47 and approximately 5% in 1963 and later years (*1–7*).

The Registry maintains a centralized continuously updated record for each cancer case. The system of multiple sources for cancer notification yields a high degree of completeness and provides a high degree of detail and accuracy of those cancer diagnoses included in the Registry. By comparing the Registry material with independent data sources, we estimated that 95–98% of all cancers diagnosed in Denmark since 1943 are included in the Registry file [Holm NV: Personal communication; (*11*)].

REPORTABLE DISEASES

Reports are requested for all cases of carcinoma, sarcoma, leukemia, Hodgkin's disease, and non-Hodgkin's lymphoma, multiple myeloma, and mycosis fungoides. In addition, notification of the following lesions is also requested: 1) papillomas of the lower urinary tract (renal pelvis, ureter, urinary bladder, and urethra), which are included with lower urinary tract cancers; 2) histologically benign tumors of the central nervous system and meninges, which are included with malignant tumors of these sites; and 3) carcinoma in situ and epithelial dysplasia of the uterine cervix, which are reported as precancerous lesions and are not tabulated with invasive cancer of the uterine cervix. Other precancerous lesions that are reported are included in the Registry material in separate categories but are not included with the respective invasive cancers (except for urinary tract papillomas and nervous system tumors).

REGISTRATION AND CODING

The information in the Danish Cancer Registry is tumor and person based. In 1968, the total material registered since 1943 was transferred to electronic data processing media. Cancers included in the Registry are identified by means of the unique personal identification number assigned by the National Central Population Registry to each individual residing in Denmark. With few exceptions every cancer diagnosis in the Registry is identified by this identity number if the person were alive on 1 April 1968, the date when the personal identification numbers were introduced. Because every new cancer reported to the Registry since 1978 is routinely cross-checked against the National Central Population Register for validation, erroneous identification is avoided.

The coding of personal data and demographic information is performed by the clerical staff of the Registry. The coding of the medical information has always been done by medical doctors or specially trained nurses under the daily supervision of the medical staff.

The original tumor codes used since 1942 could be substituted in 1958 by a modified version of the ICD-7 without too much difficulty (*12*). For greater detail than permitted by the ICD, some categories were specified differently from those adopted by the WHO (*4*). In such instances, the first digit of the 4-digit ICD code was used for the Danish specification. Over the years, the increasing demand for a higher degree of specification than given by the ICD-7 led to slight modifications and expansions of the code. [For details of the coding system, *see* (*7*).]

With an increasing number of all tumors being histologically confirmed, it was natural in 1980 for the staff to drop the modified ICD-7 and to adopt the ICD-O (*13*). All incident tumors since 1978 were coded retrospectively according to this classification after it had been modified slightly to specify the source material for the microscopic diagnosis. Comparability with the coded information in the Registry from 1943 to 1977 was maintained by a conversion program created to match the ICD-O with the modified version of the ICD-7. This computer conversion was possible because of the substantial detail provided by the combination of the three parts of the ICD-O (topography, morphology, behavior) over that given by the Registry's ICD version. Every cancer in the Registry diagnosed since 1978 is classified according to the ICD-O system and to the modified version of the ICD-7.

The modifications of the ICD-7 undertaken by the Registry have led to the following deviations from categories of the ICD-7: 1) Cancers of the rectosigmoid junction are included with the colon and not with the rectum; 2) cancer of the anal canal is grouped with skin and not with rectum; and 3) leukemias are differentiated into chronic and acute subtypes, which permits the distinction between acute nonlymphocytic leukemia and chronic lymphocytic leukemia. With these modifications, all cancers reported since 1943 are classifiable by the ICD-7 despite the fact that 3 coding systems have been in use.

MULTIPLE PRIMARY CANCERS

One of the purposes of cancer registration is measurement of the incidence of cancer occurrence in a defined population. All primary cancers reported are entered as individual cases regardless of the number of prior cancers a person might have developed. Practical difficulties in the classification of multiple tumors by cancer registries are related to the degree of certainty demanded before a new primary cancer is accepted. This problem has been stated succinctly by Clemmesen: "If we demand histological verification, we shall probably miss some cases, and if we demand differences in histological pattern in order to exclude possible metastases, we shall miss more. On the other hand, acceptance of cases without such criteria will probably result in figures which are too high" (*1*).

The Registry defines and records multiple independent primary cancers as tumors arising in different organs or, since 1978, as separate tumors with different morphologic characteristics arising in the same organ. Before 1978, a distinction was made only between carcinoma and sarcoma. The following exceptions apply: 1) Multiple tumors of the same histologic type in paired organs are included only once in the file (e.g, breast, kidney); 2) multiple tumors of the skin with identical histologies are recorded only once, even if they are located in different parts of the body. A special code indicates whether a person has had tumors on several parts of his or her body surface. Before 1978, no distinction was made between nonmelanoma types of skin cancer.

Because the Registry relies on reports from hospital departments and pathology institutes, the system depends heavily on the awareness of the physician and his assistants. For each reported cancer, it is the individual physician's responsibility to make sure that each tumor presents a defined picture of malignancy, that it is a distinct entity, and that the probability of it being a metastasis is minimal.

Underregistration could occur if hospital departments fail to notify the Registry of a new tumor in a person already reported with a prior cancer, or if the information provided is insufficient for physicians to conclude that the case was a second primary tumor. Safeguards against overregistration are part of the Registry's working procedure. Each new cancer report is compared with previous notifications for the same person. When reasonable doubt exists as to whether 2 tumors in the same person are truly independent, the diagnoses are discussed with the notifying clinical departments. Varying degrees of adherence to these rules over a 40-year registration period cannot be excluded.

The approach taken by the Registry in accepting multiple primary tumors that develop in the same person has been a conservative one; thus the number of subsequent primary cancers actually occurring may be underestimated. Although the overall completeness of the registration has been satisfactory, this may not necessarily be true for registration of second and additional primary cancers. The validity of completeness was evaluated during an ongoing case-control study of multiple primary cancers following cervical cancer (*14*). A review of approximately 4,000 hospital records for 1,886 cervical cancer patients showed that only 0.5% of the cases were incorrectly classified as cervical cancer. Among 627 patients, who, according to the Registry records, had a second primary cancer, 1.8% were erroneously coded as developing a multiple primary cancer due to errors of notification and person identification during 1943-68. By contrast, 3.8% of 1,705 women with cervical cancer were found to have developed a second primary malignant tumor that had not been reported to or recorded by the Registry. The sample of cervical cancer patients was, however, weighted with long-term survivors, and two-thirds of all unreported second primary tumors occurred 10 or more years after the diagnosis of cervical cancer. Any underreporting of second cancers is thus likely to be smaller in an unselected sample of cancer patients in whom only 15% survive for 10 years. It is also unknown whether such underreporting applies equally to second cancers following tumors of other sites, although an underreporting of hematologic cancer was observed in Denmark (*15*).

From these findings, it appears that the underreporting of second and subsequent cancers may be higher than that of all incident cancers. Although this would have little influence on the incidence rates, the effect on the observed rather than the expected number would lead to an underestimate of the relative risk in the study of second primary cancer (*16*).

FOLLOW-UP

For a registry like the Danish one covering a well-registered national population, follow-up presents a minor problem. Patients whose cancers have been registered are actively followed, and it may be safely assumed that persons who were not reported as having died are still alive. Emigration of cancer patients from Denmark is of minor importance and is not a factor in the study of second primary cancer.

Follow-up for death has been done each year since 1943 by cross-linkage with death certificates. During the major part of the Registry's existence, this was accomplished manually by comparisons of records of living persons in the Registry with all the original death certificates issued during 1 year. For all deaths occurring in 1973 and later, the linkage has been with use of the computer and the unique personal identification numbers. During linkage, the date and cause of death from the death certificate file is automatically transcribed to the Cancer Registry file. As deaths may be overlooked when a manual procedure is applied, all persons alive in 1976 were searched in the Central Population Register, which contains information on all persons who have lived in Denmark since 1 April 1968. The linkage also solved a number of problems associated with multiple entries for the same tumor, correction of birth dates, and other identifiers. All tumor records in the

TEXT-TABLE 1.—*Age-adjusted (World Standard) cancer incidence rates/100,000 population by primary site and year of diagnosis for males, Denmark, 1943–80*

ICD-7 code	Cancer site	Yr of diagnosis							
		1943–47	1948–52	1953–57	1958–62	1963–67	1968–72	1973–77	1978–80
140–148	Buccal cavity, pharynx	9.3	8.8	8.5	8.5	8.0	7.9	8.5	9.3
140	Lip	5.3	5.4	4.9	4.9	4.8	4.1	4.6	4.1
141	Tongue	0.6	0.6	0.7	0.5	0.4	0.6	0.6	0.8
142	Salivary gland	0.7	0.8	1.0	1.2	0.9	0.8	0.6	0.6
143–144	Gum, other mouth	1.0	0.9	0.8	0.7	0.7	1.2	1.2	1.6
145–148	Pharynx	1.7	1.2	1.1	1.2	1.2	1.2	1.6	2.1
150–159	Digestive system	89.6	83.1	77.2	76.5	74.0	75.1	75.2	72.3
150	Esophagus	5.7	4.5	3.5	3.2	3.0	3.2	3.5	2.9
151	Stomach	40.0	35.7	31.8	27.7	23.1	20.0	16.8	15.1
152	Small intestine	0.6	0.5	0.6	0.6	0.7	0.7	1.0	0.9
153	Colon	14.2	14.3	13.6	15.2	16.2	17.7	20.0	20.6
154	Rectum	20.3	18.4	16.8	17.9	16.7	17.0	17.2	16.1
155.0	Liver	0.6	0.9	0.7	1.2	2.5	2.7	3.0	3.4
155.1, .8	Gallbladder, other biliary	0.9	1.2	1.4	2.0	2.2	2.3	2.4	1.9
157	Pancreas	3.8	4.4	6.0	6.9	8.0	10.0	10.0	9.1
160–164	Respiratory system	15.1	21.0	27.4	36.7	46.2	56.4	62.0	64.6
160	Nasal cavities, sinuses	0.7	0.6	0.8	0.6	0.7	0.8	0.7	0.9
161	Larynx	1.6	1.9	2.3	2.6	3.5	4.2	4.6	5.4
162	Trachea, bronchus, lung	11.4	16.9	22.5	31.5	40.1	49.3	54.0	56.8
164	Mediastinum	0.4	0.5	0.3	0.4	0.3	0.2	0.4	0.3
170	Male breast	0.4	0.5	0.4	0.3	0.4	0.4	0.6	0.5
177	Prostate gland	11.5	14.7	18.0	20.0	22.5	23.1	25.9	28.4
178	Testis	3.1	3.3	3.9	4.5	5.0	5.9	7.1	8.2
180	Kidney, renal pelvis, ureter	4.4	4.7	5.5	6.3	7.8	9.2	10.2	9.2
181	Bladder, other urinary	5.9	8.0	11.1	12.9	16.6	20.7	23.4	25.9
190	Melanoma of the skin	1.2	1.5	1.7	2.4	3.0	3.7	4.9	6.1
192	Eye	1.1	1.0	0.9	1.0	1.2	1.2	0.9	1.0
193	Brain, central nervous system	5.9	6.3	6.8	8.1	8.0	8.6	9.2	9.3
194	Thyroid gland	0.4	0.6	0.5	0.8	0.8	0.9	1.1	0.9
195	Endocrine gland	0.2	0.2	0.3	0.3	0.7	0.5	0.5	0.5
196	Bone	1.2	1.0	1.0	1.1	1.0	1.2	1.1	0.7
197	Connective tissue	1.6	2.1	1.2	1.3	1.3	0.9	1.3	1.1
200–204	Lymphatic, hematopoietic system	12.2	14.0	17.0	19.2	20.7	21.5	21.5	21.3
200, 202	Non-Hodgkin's lymphoma	2.5	3.1	3.8	4.7	5.0	5.2	5.8	6.5
201	Hodgkin's disease	2.0	2.5	2.7	3.2	3.1	3.3	2.8	2.7
203	Multiple myeloma	1.1	1.3	1.9	2.5	2.9	3.1	3.0	2.7
204	Leukemias	6.5	7.0	8.4	8.7	9.5	9.8	9.6	9.3
204.0	Chronic lymphocytic	3.1	3.3	3.8	3.0	3.7	3.7	3.6	3.3
204.2, .3[a]	Acute nonlymphocytic	0.8	1.0	1.6	3.3	3.6	3.4	2.7	3.3
140–204	All sites	171.2	177.8	187.4	206.6	223.0	242.4	259.8	267.4

[a] Lymphocytic leukemias are excluded, and erythroleukemias are included.

Danish Cancer Registry are identified by a tumor number in addition to the person-identity number. Follow-up for multiple tumors can thus be accomplished easily by automated linkage of tumor records pertaining to the same persons in the Registry file.

CANCER INCIDENCE IN DENMARK, 1943–80

The age-standardized incidence rates for males and females separately [World Standard (*17*)], presented in text-tables 1 and 2 and figures 1 and 2 for 1943–80, are based on all cancers reported to the Registry irrespective of survival time (*1–7*). Total cancer incidence, excluding nonmelanoma skin cancer, has increased in males and females during the 38 years of registration starting in 1943 (*15, 18–26*). This increase is most marked among men, and, since 1970, the total age-standardized cancer incidence has been slightly higher in men than in women. The average annual increase in age-standardized incidence is 2.8 and 1.1 cases per 100,000 persons per year among men and women, respectively.

During 1943–80, the cancer pattern of Denmark has changed. Among men, stomach cancer was the leading incident cancer in the 1940s. As a result of the rapid

TEXT-TABLE 2.—*Age-adjusted (World Standard) cancer incidence rates/100,000 population by primary site and year of diagnosis for females, Denmark, 1943–80*

ICD-7 code	Cancer site	Yr of diagnosis							
		1943–47	1948–52	1953–57	1958–62	1963–67	1968–72	1973–77	1978–80
140–148	Buccal cavity, pharynx	3.0	3.0	2.8	3.1	2.9	2.5	2.5	3.1
140	Lip	0.4	0.3	0.4	0.4	0.4	0.3	0.4	0.4
141	Tongue	0.6	0.5	0.4	0.4	0.4	0.3	0.4	0.5
142	Salivary gland	0.7	1.0	1.2	1.3	1.0	0.9	0.4	0.4
143–144	Gum, other mouth	0.5	0.6	0.3	0.5	0.6	0.6	0.7	1.1
145–148	Pharynx	0.7	0.6	0.6	0.5	0.5	0.5	0.6	0.7
150–159	Digestive system	69.7	62.5	59.8	57.4	55.3	54.5	53.7	53.5
150	Esophagus	2.6	1.8	1.7	1.4	1.5	1.4	1.3	1.1
151	Stomach	29.1	23.6	20.3	16.7	12.9	10.7	8.9	7.0
152	Small intestine	0.5	0.5	0.5	0.5	0.4	0.5	0.6	0.7
153	Colon	14.8	14.9	15.2	17.0	17.6	18.6	19.8	20.5
154	Rectum	12.4	11.7	11.0	11.1	10.9	10.6	10.2	10.0
155.0	Liver	0.3	0.6	0.5	0.4	1.2	1.5	1.6	2.2
155.1, .8	Gallbladder, other biliary	2.1	2.4	3.1	3.5	3.7	3.7	3.8	3.0
157	Pancreas	3.0	3.5	4.1	4.7	5.5	6.4	6.6	7.0
160–164	Respiratory system	4.6	4.9	5.9	6.5	8.6	11.8	14.8	17.8
160	Nasal cavities, sinuses	0.4	0.3	0.3	0.3	0.3	0.3	0.3	0.5
161	Larynx	0.4	0.2	0.3	0.3	0.5	0.6	0.7	0.8
162	Trachea, bronchus, lung	2.8	3.6	4.3	5.2	7.2	10.1	12.9	15.9
164	Mediastinum	0.2	0.2	0.2	0.2	0.1	0.1	0.2	0.2
170	Female breast	42.9	44.0	44.4	45.8	49.9	54.4	61.1	62.6
171–176	Female genital	48.7	51.9	57.1	60.3	62.3	58.7	54.5	51.4
171	Cervix uteri	24.6	26.4	28.4	31.0	31.6	27.2	22.6	18.3
172	Corpus uteri	9.0	10.2	11.4	12.2	12.6	12.6	13.7	15.3
173–174	Uterus, NOS	2.2	1.1	1.6	1.2	0.7	0.7	0.5	0.5
175	Ovary, fallopian tubes	10.7	11.9	13.2	13.6	15.2	15.9	15.4	14.7
180	Kidney, renal pelvis, ureter	3.1	3.6	3.9	4.7	5.4	6.2	5.8	6.6
181	Bladder, other urinary	2.4	2.7	3.5	3.9	4.5	5.5	6.1	6.2
190	Melanoma of the skin	1.4	1.8	2.3	3.3	5.0	5.6	6.7	8.5
192	Eye	0.7	0.9	0.8	0.9	1.0	0.9	0.7	0.7
193	Brain, central nervous system	5.5	5.4	6.0	7.2	7.3	7.4	8.2	8.5
194	Thyroid gland	1.0	1.1	1.4	1.5	1.8	1.6	1.7	1.8
195	Endocrine gland	0.1	0.3	0.3	0.3	0.4	0.4	0.5	0.3
196	Bone	0.9	0.9	0.8	0.7	0.8	0.8	0.5	0.5
197	Connective tissue	1.3	1.7	1.2	1.1	1.1	0.9	1.1	0.7
200–204	Lymphatic, hematopoietic system	8.8	10.1	11.1	12.6	13.1	14.1	14.2	14.2
200, 202	Non-Hodgkin's lymphoma	1.9	2.0	2.4	3.1	3.5	3.7	3.9	4.5
201	Hodgkin's disease	1.5	1.7	1.8	2.0	1.9	2.1	1.7	1.7
203	Multiple myeloma	0.9	1.1	1.4	1.7	2.0	2.0	2.2	1.9
204	Leukemia	4.5	5.2	5.5	5.8	5.6	6.1	6.4	6.0
204.0	Chronic lymphocytic	1.7	1.8	1.7	1.6	1.6	1.6	1.6	1.5
204.2, 3[a]	Acute nonlymphocytic	0.6	0.9	1.1	2.5	2.6	2.6	2.4	2.3
140–204	All sites	204.6	202.6	208.4	217.0	224.6	229.8	237.3	242.2

[a] Lymphocytic leukemias are excluded, and erythroleukemias are included.

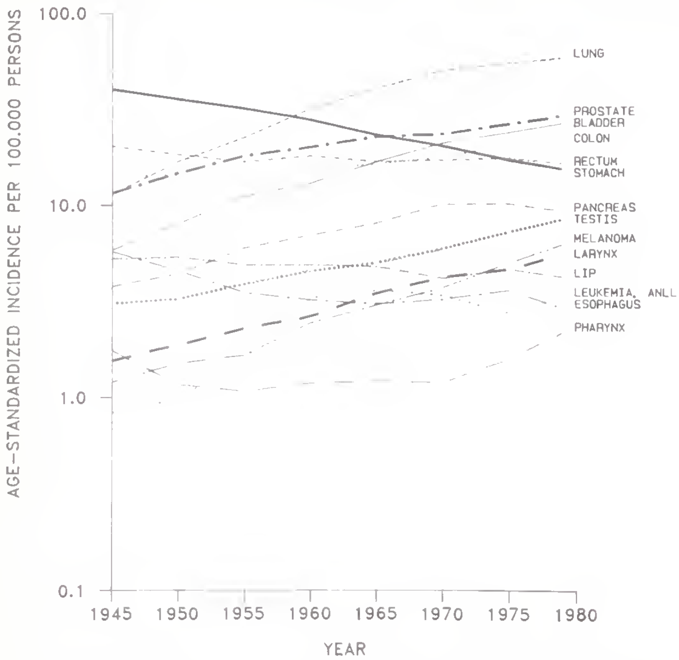


FIGURE 1.—Age-standardized incidence rates/100,000 persons by primary site and year of diagnosis for males, Denmark, 1943–80. ANLL = acute nonlymphocytic leukemia.

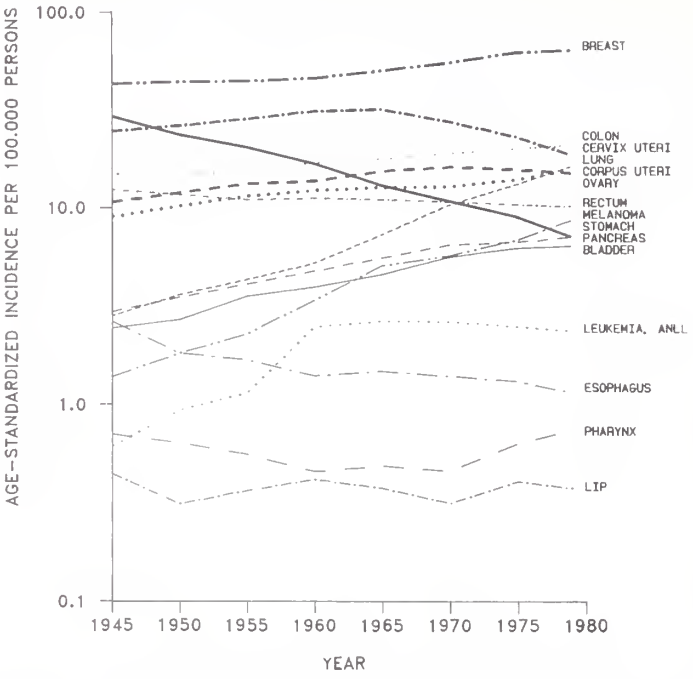


FIGURE 2.—Age-standardized incidence rates/100,000 persons by primary site and year of diagnosis for females, Denmark, 1943–80.

decrease in stomach cancer incidence and of the increase in lung cancer, the latter type is now by far the leading cancer among men. Lung cancer rates are followed by cancers of the prostate, bladder (including papilloma), colon, and rectum. Among women, breast is the most common site and has been so throughout the period of registration. Similar to the trend seen among men, stomach cancer, which was in second position in 1945, has also decreased rapidly and is no longer among the 10 most frequent cancers found in women. A decrease has also occurred for cancer of the cervix uteri since around 1965, which is probably partly related to population-based mass screening (*27*). Increasing risks are observed for a number of sites, most notably cancers of the lung and bladder and malignant melanoma.

These changing trends in the incidence of cancer over the relatively short period of four decades are indicators of the influence of environmental factors on the risk of cancer development. Changes in diagnostic procedures and the increased use of medical facilities, in particular by the elderly, may also affect the interpretation of incidence trends.

VALIDITY OF CANCER DIAGNOSES

The degree of verification for all cancers notified to the Registry during the period 1943–80 is presented in text-table 3. The proportion of cases verified by histologic examination increased from just over 50% in the mid-1940s to 90% around 1980. Correspondingly, the proportion of cases known to the Registry only from death certificates decreased gradually from around 20% in 1943–47 to less than 6% after 1968. A similar decrease was noted for clinically and surgically verified cases that were not micro-

TEXT-TABLE 3.—*Percent distribution of method of confirmation for all cancers combined by year of diagnosis for males and females, Denmark, 1943–80*

Type of confirmation	Yr of diagnosis								
	1943–47	1948–52	1953–57	1958–62	1963–67	1968–72	1973–77	1978–80	All years
	No. of cancers in interval								
	49,144	55,439	64,238	74,043	86,902	103,282	118,118	79,921	631,087
Microscopically confirmed									
Without autopsy	37.1	43.3	43.8	46.6	48.9	50.5	54.6	65.6	50.2
With autopsy	15.6	19.6	24.3	29.0	32.0	35.2	31.8	24.8	28.0
Not microscopically confirmed									
Clinical report only	23.5	20.8	18.0	14.4	11.0	7.9	6.9	7.6	12.2
Autopsy report only	4.6	2.6	2.3	2.0	2.0	1.9	1.8	0.7	2.1
Death certificate report only	19.3	13.7	11.7	8.0	6.1	4.5	5.0	1.3	7.5

scopically confirmed. The fraction of cases diagnosed at autopsy without histologic confirmation has remained virtually the same over the years. When subdividing the cases with histologic verification with regard to whether an autopsy report was available to the Registry, it was found that the proportion with autopsies increased from 15.6% in 1943-47 to 35.2% in 1968-72 and then decreased to 24.8% in 1978-80. The slightly higher proportion of autopsies recorded among cancer deaths and the apparent decrease in autopsies in the last years of the period are likely due to the high number of cancer patients still alive in 1980. As a result of the criteria for selection of case material for the study of multiple primary cancers (*16*), the proportion of cases confirmed solely on the basis of death certificates can only decrease compared with the data presented in text-table 3. Thus the confirmation percentages associated with the other types of verification must increase accordingly.

CONCLUSIONS

A population-based cancer registry like the Danish one that covers a well-defined national population with free access to good medical care is well suited for the study of multiple primary cancers. Cancer patients are followed for life, with virtually no loss to follow-up. The same tumor classification system has been used during all of the period 1943-80, and the incidence rates used for calculation of expected numbers of second primary cancers are derived from the same population from which the first primary cancer arose.

Comparisons of the cancer Registry cases with information from external data sources have indicated a high validity of the site-specific diagnoses and a high degree of completeness. These comparisons have also indicated that irregularities in notification and coding and a conservative approach to acceptance of subsequent tumors in cancer patients should be borne in mind when the results of the study of second primary cancer are interpreted. For example, multiple tumors of the same histologic type in paired organs such as the breast are recorded only once. The possible misclassification of metatases and the possible effect of a slightly higher autopsy rate among cancer patients than for deaths overall may lead to some overestimates, but, on balance, the true risk of second cancer development is probably underestimated.

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Second Cancer Following Cancers of the Buccal Cavity and Pharynx in Denmark, 1943–80 [1]

Geert Schou, Hans H. Storm, *and* Ole M. Jensen [2]

ABSTRACT—Cancers of the buccal cavity and the pharynx are not only anatomically related but, except for the nasopharynx, also have risk factors in common. Multifocal occurrence of cancers in the buccal cavity and pharynx must be kept in mind when one is interpreting findings on multiple tumors. However, susceptibility to common risk factors, predominantly alcohol and tobacco, seem to be in operation among males, inasmuch as excess lung cancer followed cancers of the tongue [relative risk (RR) = 2.2], other parts of the mouth (RR = 2.2), and pharynx (RR = 2.0). Among females, lung cancer was in excess after cancers of the tongue (RR = 3.7) and mouth (RR = 3.6). Among males, esophageal cancer was elevated after cancers of the mouth (RR = 4.7) and tongue (RR = 5.7). Other combinations of tobacco-related cancers among males include those of the bladder (RR = 2.5) after cancer of the tongue and larynx (RR = 5.4) after pharyngeal cancer. Common etiologic factors or the multifocal nature of tumors of the buccal cavity might also account for the increases of cancer of the mouth (RR = 2.6) following lip cancer and cancer of the tongue (RR = 14) following mouth cancers among males. Among females, cancer of the mouth (RR = 17) was elevated after tongue, tongue (RR = 31) after mouth, and tongue (RR = 10) after salivary gland tumors. The excess of pharyngeal cancers in women (RR = 19) following cancer of the lip may be explained by common risk factors. Observed deficits of colon cancer following cancer of the lip in males and after tongue and salivary gland tumors in females could reflect low socioeconomic status, although a deficit of stomach cancer among males (RR = 0.1) also followed cancer of the salivary glands.—Natl Cancer Inst Monogr 68: 253-276, 1985.

LIP (ICD-7, 140)

Cancers of the lip account for 1.2% of all malignant tumors in Denmark, excluding nonmelanoma skin cancers. Lip cancer is approximately ten times more frequent among men than women, and the risk for males is about four times higher in rural districts than in the city of Copenhagen (*1*). The age-standardized incidence rates for men have decreased slightly from 5.3 in 1943–47 to 4.1/100,000 in 1978–80, whereas they remained stable at 0.4/100,000 for women. The survival following cancer of the lip is excellent. In Norway, the relative survival rate is close to 100% (*2*). The Danish Cancer Registry tumor classification distinguishes between cancers of the red portion of the lip (ICD-7, 140) and cancers of the skin of lip (ICD-7, 191). Cases reported to the Registry with no indication whether it was skin or the red portion of the lip are likely to be coded as lip cancers. The lip category may then include some nonmelanoma skin cancers, but the magnitude of this problem is unknown. This potential source of error in notification and coding of lip cancers should be kept in mind because the factors for secondary cancer development may not be similar for nonmelanoma skin cancers and true lip cancers.

The predominant risk factor for cancer of the lip is use of tobacco, especially pipe smoking (*3, 4*). Alcohol consumption has also been implicated (*3, 5*) as have low social class (*3, 6, 7*), and related factors such as poor dentition and chronic irritation or inflammation of the lip mucosa (*7*). Leukoplakias are often found coexistent with cancers of the lip (*8*). Occupational groups such as sailors and farmers who are exposed to sunlight experience a higher risk for lip cancer than do those in the general population (*9, 10*).

Results

During 1943–80, a total of 5,505 persons (5,054 men and 451 women) with cancer of the lip were reported to the Registry and included in the study. The average age at diagnosis was 62 years for males and 66 years for females. The average follow-up was 10.7 years; we determined 58,763 person-years as the basis for calculating the expected numbers of second tumors. Most of the patients (79%) received radiotherapy as part of their initial treatment, and approximately 30% of those with lip cancer were treated by surgery.

Among persons who developed multiple primary cancers, 82% of the first and 76% of the second cancers were verified histologically. More than 20% of the second primary cancers were verified only by clinical means or death certificates. A total of 613 second primary cancers were observed in men, whereas 695 were to be expected on the basis of rates prevailing in the general population (RR = 0.88; 95% CI = 0.81–0.96). Among women, 52 second primary cancers were observed versus 48 expected (RR = 1.08; 95% CI = 0.81–1.4). Reduction of the total observed and expected numbers by the contributions assigned to lip cancer did not affect these estimates.

The risk of cancer of the mouth was significantly increased for males (RR = 2.6; 95% CI = 1.1–5.2), for which the excess was primarily observed during the first 10 years of observation. A high risk of pharyngeal cancer among women with lip cancer was based on only 2 cases.

ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; RR = relative risk(s); CI = confidence interval.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] The Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Geert Schou.

Significant deficits were observed among men for cancers of the colon (RR = 0.7) and prostate (RR = 0.8). The risk for second primary pancreatic cancer was also decreased though not significantly (RR = 0.7). No other significant excesses or deficits were seen.

Discussion

Perhaps the most striking finding is the overall deficit of second cancer development following cancer of the lip. Apart from possible underreporting, the rural predominance of lip cancer may be responsible for this low rate because all other cancers in Denmark occur with pronounced excesses in the urban regions of the country (*1*). The fact that none of the tobacco- and alcohol-related cancers outside the oral cavity (larynx, lung, and esophagus) were observed in excess is puzzling. The lack of association may partially be explained if differences in types of tobacco used yield different risk patterns. Although cancer of the lip is strongly associated with pipe smoking, possibly in combination with UV light (*10*), other tobacco-related tumors have cigarette smoke as the major risk factor. The probable inclusion of skin cancer with cancer of the lip, however, must be kept in mind. Skin cancer is not known to be related to smoking habits, and thus the inappropriate inclusion of cancers of the skin would dilute the possibility of our finding excesses of smoking-related tumors. The observed deficit of colon cancers is unexplained.

TONGUE (ICD-7, 141)

The tongue is a rare site for cancer, accounting for only 0.2% of all cancers in Denmark. The age-standardized incidence rates for both sexes, 0.6 and 0.4/100,000 for men and women, respectively, remained stable during 1943–80. Cancer of the tongue is three to five times more frequent among males and females in Copenhagen than in rural areas, with rates for persons living in provincial towns in the intermediate range (*1*).

Etiologic factors are to a large degree common for cancer of the oral cavity, with higher rates for low income groups (*3, 6*). The major risk factors in Denmark are tobacco smoking and alcohol, acting separately or in combination (*4, 11*). The habits of tobacco chewing or snuff dipping also increase the risk of oral cavity cancer (*10*). Nutritional deficiences which might be related to social class have also been implicated (*7*). Leukoplakia is often found coincidentally with cancer of the tongue and is regarded as a precancerous lesion (*8*).

Survival is poorer among males than females. The relative 5-year survival rates for men and women in Norway are 36 and 45%, respectively (*2*).

Results

A total of 1,107 persons with tongue cancers were reported to the Registry during 1943–80. The number of cases included in the study did not differ substantially by sex. The average age at diagnosis was 66 years, and the average follow-up was 4.3 years. Most of the patients (71%) received radiation as part of their initial treatment.

Histologic confirmation was received for 88% of the second primary cancers and 97% of their corresponding first primary cancers. For both sexes combined, 68 second primary cancers were found (RR = 1.18; 95% CI = 0.92–1.50). Among men a total of 43 second primaries occurred versus 30.1 expected (RR = 1.4; 95% CI = 1.0–1.9), whereas 25 were observed in women in contrast to 27.5 expected (RR = 0.9; 95% CI = 0.6–1.3).

For both sexes combined, a strongly increased risk of subsequent cancer of the mouth was shown (RR = 12.0; 95% CI = 2.4–35). Significantly increased risks of cancers of the esophagus (RR = 5.7), lung (2.2), and kidney (4.2) were observed among men. The excess of esophageal cancer was primarily seen 10 or more years after the diagnosis of tongue cancer, whereas the increase in the risk of kidney cancer was most pronounced during the first 4 years after the tongue cancer diagnosis. The risk of bladder cancer (RR = 2.5) was elevated among men, though not significantly.

Among women, the RR of new cancers in the mouth was increased (16.9; 95% CI = 1.9–60), as was lung cancer (3.7; 95% CI = 1.0–9.5). In contrast, a decrease in the risk of cancers of the stomach and colon was suggested. These deviations were not statistically significant, but by combining all cancers of the digestive system in women, we noted a deficit based on 4 cases observed and 11 expected (RR = 0.4; 95% CI = 0.1–0.9).

Discussion

The overall increased risk of second primary cancers among men with tongue cancer is mainly attributable to cancers of the esophagus, lung, kidney, and urinary bladder. The findings resemble previous studies of multiple primary cancers in the oral cavity (*12, 13*). Tobacco is a recognized risk factor for all of these sites, and alcohol has a potentiating effect for cancer of the esophagus (*5*). The excess of esophageal cancer tended to occur 10 or more years after primary diagnosis, which suggests a possible influence of radiotherapy. The excess of cancers within the mouth is consistent with the multicentric nature of cancers of the buccal cavity and pharynx (*12*) and common etiologic factors such as tobacco and alcohol consumption. Some second tumors might be due to radiotherapy or to misdiagnosis of metastatic lesions. The high RR of second tumors in the buccal cavity indicates the need for continued clinical surveillance of patients with cancer of the tongue. The low RR of cancer of the digestive tract is unexplained.

SALIVARY GLANDS (ICD-7, 142)

Cancer of the salivary glands comprises only 0.2% of all tumors in Denmark (*14*) and includes a mixture of neoplasms: adenocarcinomas (Cylindroma), mixed tumors reported as benign or malignant, Warthin's tumor (papillary cystadenoma lymphomatosum), and mucoepidermoid tumors. The completeness of notification of these tumors is unknown.

In 1958–62, the age-standardized incidence rates were 1.2 and 1.3/100,000 for men and women, respectively, and they decreased thereafter to 0.6 and 0.4/100,000 in recent years. In 1980, the incidence rates for men in Copenhagen were twice as high as those for men in rural areas. No substantial urban–rural difference was seen for women.

The causation of cancer of the major salivary glands is largely unknown, although ionizing radiation has been linked to some cases (*15*). Survival after a salivary gland cancer, as reported in Norway, is favorable; the relative 5-year survival rate is 66% for men and 83% for women (*2*).

Results

A total of 1,753 salivary gland tumors, 823 among males and 930 among females, occurred during 1943–80 in Denmark and were included in the study. The average follow-up time was 11.2 years, and 149 (or 8.5%) persons developed a second primary cancer (RR = 1.0; 95% CI = 0.8–1.1). Although most of the patients with salivary gland tumors apparently do not respond well to radiotherapy (*16*), 66% received radiation as part of their initial treatment. Over 83% of the second primary cancers were histologically verified in contrast to only 69% of the initial salivary gland tumors.

No individual site occurred significantly above or below expectation following salivary gland cancer among men. Nonsignificant increases among men were seen for cancers of the esophagus (RR = 2.0), nasal cavity (RR = 5.4), kidney (RR = 1.8), and brain (RR = 3.1), whereas stomach cancer was decreased (RR = 0.1). Women showed significantly increased risks for cancers of the tongue (RR = 10.3; 95% CI = 1.2–38). Thyroid cancer was also increased (RR = 6.6; 95% CI = 1.8–17) particularly among long-term survivors, whereas colon cancer was in deficit (RR = 0.3; 95% CI = 0.1–0.9). A nonsignificant RR of 1.3 for second primary breast cancer was seen. Breast cancer increased slightly with time since diagnosis, but the trend was not significant.

Discussion

Cancer of the salivary glands is rare, and the confidence limits about the RR of second tumor development for individual sites are necessarily wide. However, a tendency is apparent for excesses of alcohol- and tobacco-related cancers to develop, such as for the tongue, esophagus, respiratory tract, and kidney. The present findings suggest etiologic similarities between these sites and salivary gland cancers, although tobacco and alcohol have not previously been implicated as risk factors for tumors in the salivary glands. An increased risk of lung cancer following salivary gland cancer was previously observed in Connecticut (*17*) and England (*18*).

The association reported between salivary gland cancer and breast cancer (*18, 19*) finds little support from this cohort study, which is more in line with another investigation showing no relationship (*20*). The excess of tongue cancer may be explained in part by multifocal appearances of cancer within the buccal cavity, especially because the tongue cancers occurred within 5 years of the primary salivary gland diagnosis. Increased medical surveillance may also have contributed to this excess. The increased risk of thyroid cancer among long-term survivors is interesting, inasmuch as two-thirds of the patients with salivary gland tumors were treated with radiation. Although the doses reaching the thyroid gland may be small, the role of radiotherapy remains a possibility.

MOUTH (ICD-7, 143, 144)

Cancers of the mouth are infrequent in Denmark and account for only 0.5% of all tumors in men and 0.4% in women. The age-standardized incidence rates were 1.6/100,000 for men and 1.1 for women in 1978–80. Incidence rates in Copenhagen are two to three times higher than in rural areas (*1*). The incidence rates of mouth cancer among men and women decreased slightly during 1943–57 but increased slightly afterward.

As for the other sites within the buccal cavity and pharynx, the major risk factors for cancers of the mouth are tobacco smoking (*3, 4, 11*), alcohol (*6, 7, 11*), low socioeconomic status (*3, 6*), probably nutritional deficiences (*7*), leukoplakia, and erythroplasia (*8*). Tumors of the buccal cavity tend to be multifocal, which leads to elevated risks for neighboring sites. Survival depends on the localization of the cancer in the mouth, and the 5-year relative survival rate varies from 27% for cancers of the floor of the mouth among men to 62% for oral cancers other than the floor of the mouth among women (*2*). Survival tends to be better for women than for men.

Results

Altogether, 1,764 cancers of the mouth occurred between 1943 and 1980. Radiation was part of the initial treatment to most patients (76%). More than 81% of the second primary cancers and 94% of the corresponding initial mouth cancers were histologically verified. The percentage of second primary cancers diagnosed only on death certificates (4.6%) is close to the average for all sites combined.

Second primary cancers developed in 131 persons (7.4%) following cancer of the mouth (RR = 1.3; 95% CI = 1.1–1.6). Significant excesses for all sites combined occurred only among men. Increased risks for cancer of the lip (RR = 6.8), tongue (13.9), mouth (7.1), esophagus (4.7), and lung (2.2) were seen among men, but a decreased risk was noted for cancer of the prostate (0.4). In women, a significantly increased risk was seen for cancers of the tongue (RR = 31), esophagus (6.9), and lung (3.6).

Discussion

The overall excess of second cancers following tumors of the mouth is mainly due to increased risk of alcohol- and tobacco-related cancers and is in line with the results of other studies (*12, 13*). The excess cancers of the tongue may also be explained by the tendency to multifocal lesions that was probably influenced by the combined action of alcohol and tobacco, which is also likely to account for the increased risk of esophageal cancer (*5, 11*). In a previous study, an excess of prostate cancer was observed following mouth cancer (*17*), but this association was not confirmed in our data.

PHARYNX (ICD-7, 145, 148)

Cancers of the pharynx are uncommon, accounting for only 0.4% of all cancers diagnosed in 1980 in Denmark (*14*). The age-standardized incidence for both men and women were almost as high in 1943–47 as in 1978–80 (men 2.1 and women 0.7/100,000), with lower rates occurring between these 2 periods. The risk of pharyngeal cancer is about three times higher among men than among women, and rates among men are approximately four times higher in Copenhagen than in rural areas. No substantial urban–rural difference is seen among women.

Similar to oral cancers, the risk of pharyngeal cancer has been linked to alcohol and tobacco use (*3, 7, 11*). Less specific risk factors include low socioeconomic status (*6, 7*), nutritional deficiences, and occupation (*7*). The etiology of nasopharyngeal cancer differs from that of the remainder of the pharynx (*21*); because of its rarity in Denmark, nasopharyngeal cancer has been combined in the present analysis with other tumors of the pharynx (*1*). The pharynx thus can be subdivided into the tonsils, oral mesopharynx, nasopharynx, and hypopharynx, each with different survival patterns. Of the four, the poorest 5-year relative survival rates were for cancer of the hypopharynx: 17% for men and 28% for women. No major differences in survival after cancers of the nasopharynx and mesopharynx have been observed (*2*).

Results

Between 1943 and 1980, the Registry received reports of 1,857 patients with primary pharyngeal cancer who were included in this study. No major differences were observed between the 1,289 males and 568 females with respect to the development of second primary cancers (males 4%, females 3%) or mean age at diagnosis (61 yr). However, females on the average were followed slightly longer than males (males 2.9 yr, females 3.8 yr). The total follow-up was 3,743 and 2,168 person-years for males and females, respectively. Among the 68 second primary cancers, 59 were histologically confirmed, whereas 66 of the preceding pharyngeal cancers were histologically confirmed.

Second primary cancers were reported in 51 males, whereas 36.4 were expected (RR = 1.4; 95% CI = 1.0–1.8). Among women, the 17 observed second cancers were not statistically different from expectation (RR = 0.9; 95% CI = 0.5–1.4). Although numbers were small, significant excesses of second cancers of the larynx (RR = 5.4; 95% CI = 1.1–16) and lung (RR = 2.0; 95% CI = 1.1–3.4) were observed among men. Nonsignificant elevations were indicated for cancers of the mouth, esophagus, and kidney. High RR for cancers of the thyroid and testis were based on only single observed cancers.

Discussion

The overall excess of second cancer development among men is mainly confined to sites in the buccal cavity, esophagus, larynx, lung, and kidney. Tobacco (*3, 4*) and in some instances alcohol (*5, 11*) are known to play a part in the etiology of these sites as well as for pharyngeal cancer (*3, 4, 11*). Other excesses and deficits are probably due to small numbers and the play of chance alone.

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LIP
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the lip, 1943-80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	5,054	451	5,505
No. who developed a second primary cancer	613	52	665
Average age at diagnosis of first cancer, yr	62	66	62
Average yr of diagnosis of first cancer	1963	1964	1963
Person-yr of follow-up	54,484	4,279	58,763
Average follow-up, yr	10.8	9.5	10.7
Percent given radiotherapy for first cancer	80	71	79

[a] ICD-7 code = 140.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the lip in Denmark, 1943-80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	418	62.9
Only the first cancer	124	18.6
Only the second cancer	86	12.9
Neither first nor second cancer	37	5.6
Total second primary cancers	665	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LIP
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the lip among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,505			5,148			3,679			2,422			5,505		
Person-yr in interval	5,347			17,524			15,012			20,880			58,763		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**43**	**55.58**	**0.8**	**178**	**191.44**	**0.9**	**158**	**180.13**	**0.9**	**286**	**315.77**	**0.9**	**665**	**742.92**	**0.9**[b]
All excluding site of initial cancer	**42**	**54.60**	**0.8**	**178**	**188.16**	**0.9**	**157**	**177.18**	**0.9**	**285**	**311.18**	**0.9**	**662**	**731.11**	**0.9**[b]
Buccal cavity, pharynx	**3**	**1.81**	**1.7**	**5**	**6.06**	**0.8**	**6**	**5.45**	**1.1**	**5**	**8.70**	**0.6**	**19**	**22.03**	**0.9**
Lip	1	0.98	1.0	0	3.28	0.0	1	2.95	0.3	1	4.59	0.2	3	11.81	0.3[b]
Tongue	1	0.14	7.1	0	0.48	0.0	2	0.43	4.7	0	0.64	0.0	3	1.69	1.8
Salivary gland	0	0.15	0.0	1	0.52	1.9	1	0.48	2.1	0	0.75	0.0	2	1.91	1.0
Gum, other mouth	1	0.25	4.0	3	0.85	3.5	2	0.78	2.6	2	1.38	1.4	8	3.27	2.4[b]
Pharynx	0	0.28	0.0	1	0.92	1.1	0	0.82	0.0	2	1.34	1.5	3	3.36	0.9
Digestive system	**12**	**22.35**	**0.5**[b]	**77**	**75.94**	**1.0**	**68**	**69.95**	**1.0**	**108**	**115.55**	**0.9**	**265**	**283.79**	**0.9**
Esophagus	1	1.04	1.0	3	3.43	0.9	2	3.02	0.7	6	4.62	1.3	12	12.10	1.0
Stomach	4	7.58	0.5	31	25.18	1.2	23	22.46	1.0	44	32.91	1.3	102	88.13	1.2
Colon	1	4.96	0.2	17	17.17	1.0	17	16.22	1.0	18	29.36	0.6[b]	53	67.72	0.8
Rectum	3	4.87	0.6	13	16.53	0.8	16	15.24	1.0	23	25.05	0.9	55	61.69	0.9
Liver, biliary	0	1.11	0.0	7	3.94	1.8	3	3.83	0.8	5	7.37	0.7	15	16.26	0.9
Pancreas	2	2.05	1.0	5	7.18	0.7	4	6.99	0.6	8	12.97	0.6	19	29.18	0.7
Respiratory system	**9**	**9.58**	**0.9**	**27**	**33.65**	**0.8**	**31**	**32.58**	**1.0**	**65**	**61.39**	**1.1**	**132**	**137.21**	**1.0**
Nasal cavities, sinuses	0	0.16	0.0	0	0.53	0.0	0	0.49	0.0	2	0.78	2.6	2	1.96	1.0
Larynx	0	0.68	0.0	0	2.34	0.0	0	2.20	0.0	1	3.94	0.3	1	9.16	0.1[b]
Trachea, bronchus, lung	9	8.28	1.1	27	29.13	0.9	29	28.28	1.0	60	53.82	1.1	125	119.51	1.0
Female breast	1	0.85	1.2	4	2.73	1.5	1	2.38	0.4	4	3.34	1.2	10	9.30	1.1
Female genital tract	**1**	**0.71**	**1.4**	**3**	**2.26**	**1.3**	**2**	**1.89**	**1.1**	**3**	**2.53**	**1.2**	**9**	**7.39**	**1.2**
Cervix uteri	0	0.21	0.0	2	0.67	3.0	0	0.53	0.0	1	0.65	1.5	3	2.07	1.5
Corpus uteri	0	0.20	0.0	0	0.64	0.0	1	0.54	1.9	1	0.75	1.3	2	2.12	0.9
Uterus, NOS	0	0.02	0.0	0	0.07	0.0	0	0.06	0.0	0	0.08	0.0	0	0.24	0.0
Ovary, fallopian tubes	1	0.22	4.6	1	0.69	1.4	0	0.59	0.0	0	0.82	0.0	2	2.32	0.9
Prostate gland	6	6.88	0.9	20	24.48	0.8	17	24.06	0.7	36	45.99	0.8	79	101.41	0.8[b]
Testis	0	0.22	0.0	3	0.70	4.3	1	0.58	1.7	1	0.77	1.3	5	2.25	2.2
Kidney, renal pelvis, ureter	1	1.71	0.6	7	5.95	1.2	3	5.71	0.5	7	10.37	0.7	18	23.74	0.8
Bladder, other urinary	5	3.99	1.3	10	14.05	0.7	15	13.63	1.1	23	26.18	0.9	53	57.85	0.9
Melanoma of the skin	1	0.46	2.2	1	1.59	0.6	1	1.48	0.7	4	2.55	1.6	7	6.09	1.1
Eye	0	0.17	0.0	0	0.59	0.0	0	0.53	0.0	0	0.86	0.0	0	2.16	0.0
Brain, central nervous system	1	0.89	1.1	4	3.00	1.3	2	2.73	0.7	4	4.35	0.9	11	10.98	1.0
Thyroid gland	0	0.17	0.0	1	0.60	1.7	0	0.57	0.0	2	0.95	2.1	3	2.28	1.3
Bone	0	0.11	0.0	0	0.36	0.0	0	0.33	0.0	1	0.51	2.0	1	1.31	0.8
Connective tissue	0	0.21	0.0	1	0.72	1.4	1	0.62	1.6	0	0.92	0.0	2	2.46	0.8
Lymphatic, hematopoietic system	**2**	**3.45**	**0.6**	**12**	**12.02**	**1.0**	**8**	**11.52**	**0.7**	**16**	**20.53**	**0.8**	**38**	**47.52**	**0.8**
Non-Hodgkin's lymphoma	0	0.89	0.0	4	3.10	1.3	2	2.96	0.7	2	5.26	0.4	8	12.19	0.7
Hodgkin's disease	0	0.25	0.0	0	0.87	0.0	0	0.79	0.0	1	1.25	0.8	1	3.16	0.3
Multiple myeloma	0	0.63	0.0	1	2.22	0.5	3	2.17	1.4	4	3.98	1.0	8	9.01	0.9
Leukemias	1	1.64	0.6	7	5.71	1.2	3	5.48	0.5	9	9.84	0.9	20	22.69	0.9
Chronic lymphocytic	1	0.91	1.1	4	3.21	1.2	2	3.08	0.6	7	5.52	1.3	14	12.73	1.1
Acute nonlymphocytic	0	0.36	0.0	3	1.26	2.4	0	1.23	0.0	2	2.47	0.8	5	5.31	0.9

[a] ICD-7 code = 140.

[b] $P < .05$.

LIP
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the lip among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,054			4,745			3,409			2,252			5,054		
Person-yr in interval	4,918			16,177			13,921			19,469			54,484		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**40**	**51.27**	**0.8**	**162**	**177.41**	**0.9**	**146**	**167.82**	**0.9**	**265**	**298.49**	**0.9**	**613**	**694.99**	**0.9^{b}**
All excluding site of initial cancer	**39**	**50.30**	**0.8**	**162**	**174.16**	**0.9**	**146**	**164.90**	**0.9**	**264**	**293.94**	**0.9**	**611**	**683.29**	**0.9^{b}**
Buccal cavity, pharynx	**3**	**1.75**	**1.7**	**4**	**5.86**	**0.7**	**5**	**5.28**	**0.9**	**4**	**8.45**	**0.5**	**16**	**21.35**	**0.7**
Lip	1	0.97	1.0	0	3.25	0.0	0	2.92	0.0	1	4.55	0.2	2	11.70	0.2^{b}
Tongue	1	0.13	7.7	0	0.44	0.0	2	0.40	5.0	0	0.59	0.0	3	1.56	1.9
Salivary gland	0	0.14	0.0	1	0.48	2.1	1	0.45	2.2	0	0.71	0.0	2	1.78	1.1
Gum, other mouth	1	0.23	4.3	3	0.79	3.8	2	0.73	2.8	2	1.30	1.5	8	3.06	2.6^{b}
Pharynx	0	0.27	0.0	0	0.89	0.0	0	0.79	0.0	1	1.30	0.8	1	3.25	0.3
Digestive system	**12**	**20.69**	**0.6**	**71**	**70.46**	**1.0**	**63**	**65.08**	**1.0**	**100**	**108.77**	**0.9**	**246**	**264.99**	**0.9**
Esophagus	1	0.99	1.0	3	3.26	0.9	2	2.87	0.7	6	4.41	1.4	12	11.53	1.0
Stomach	4	7.10	0.6	28	23.62	1.2	22	21.10	1.0	40	31.24	1.3	94	83.06	1.1
Colon	1	4.47	0.2	15	15.53	1.0	14	14.74	0.9	15	27.15	0.6^{b}	45	61.89	0.7^{b}
Rectum	3	4.59	0.7	12	15.62	0.8	16	14.44	1.1	22	23.94	0.9	53	58.59	0.9
Liver, biliary	0	0.98	0.0	7	3.50	2.0	2	3.42	0.6	5	6.74	0.7	14	14.64	1.0
Pancreas	2	1.89	1.1	5	6.67	0.7	4	6.52	0.6	8	12.25	0.7	19	27.33	0.7
Respiratory system	**8**	**9.38**	**0.9**	**27**	**32.99**	**0.8**	**30**	**31.98**	**0.9**	**63**	**60.48**	**1.0**	**128**	**134.83**	**0.9**
Nasal cavities, sinuses	0	0.15	0.0	0	0.51	0.0	0	0.47	0.0	2	0.76	2.6	2	1.89	1.1
Larynx	0	0.67	0.0	0	2.31	0.0	0	2.18	0.0	1	3.91	0.3	1	9.07	0.1^{b}
Trachea, bronchus, lung	8	8.11	1.0	27	28.58	0.9	28	27.78	1.0	58	53.05	1.1	121	117.52	1.0
Prostate gland	6	6.88	0.9	20	24.48	0.8	17	24.06	0.7	36	45.99	0.8	79	101.41	0.8^{b}
Testis	0	0.22	0.0	3	0.70	4.3	1	0.58	1.7	1	0.77	1.3	5	2.25	2.2
Kidney, renal pelvis, ureter	1	1.60	0.6	7	5.59	1.3	3	5.39	0.6	6	9.90	0.6	17	22.48	0.8
Bladder, other urinary	5	3.87	1.3	10	13.65	0.7	14	13.27	1.1	22	25.63	0.9	51	56.42	0.9
Melanoma of the skin	1	0.41	2.4	1	1.43	0.7	0	1.34	0.0	4	2.35	1.7	6	5.54	1.1
Eye	0	0.16	0.0	0	0.55	0.0	0	0.50	0.0	0	0.82	0.0	0	2.04	0.0
Brain, central nervous system	1	0.82	1.2	3	2.79	1.1	2	2.55	0.8	4	4.09	1.0	10	10.26	1.0
Thyroid gland	0	0.14	0.0	1	0.50	2.0	0	0.48	0.0	2	0.82	2.4	3	1.94	1.5
Bone	0	0.10	0.0	0	0.34	0.0	0	0.31	0.0	1	0.48	2.1	1	1.23	0.8
Connective tissue	0	0.20	0.0	1	0.67	1.5	1	0.58	1.7	0	0.87	0.0	2	2.32	0.9
Lymphatic, hematopoietic system	**2**	**3.23**	**0.6**	**11**	**11.28**	**1.0**	**8**	**10.86**	**0.7**	**15**	**19.54**	**0.8**	**36**	**44.91**	**0.8**
Non-Hodgkin's lymphoma	0	0.82	0.0	4	2.88	1.4	2	2.76	0.7	2	4.96	0.4	8	11.41	0.7
Hodgkin's disease	0	0.24	0.0	0	0.82	0.0	0	0.75	0.0	1	1.19	0.8	1	3.00	0.3
Multiple myeloma	0	0.59	0.0	1	2.07	0.5	3	2.04	1.5	3	3.78	0.8	7	8.48	0.8
Leukemias	1	1.54	0.6	6	5.40	1.1	3	5.20	0.6	9	9.42	1.0	19	21.57	0.9
Chronic lymphocytic	1	0.87	1.1	4	3.06	1.3	2	2.94	0.7	7	5.31	1.3	14	12.19	1.1
Acute nonlymphocytic	0	0.33	0.0	2	1.18	1.7	0	1.16	0.0	2	2.35	0.9	4	5.01	0.8

[a] ICD-7 code = 140.

[b] $P < .05$.

LIP
FEMALES

TABLE 1E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the lip among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	451			403			270			170			451		
Person-yr in interval	430			1,347			1,091			1,411			4,279		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	3	**4.31**	**0.7**	**16**	**14.03**	**1.1**	**12**	**12.31**	**1.0**	**21**	**17.28**	**1.2**	**52**	**47.93**	**1.1**
All excluding site of initial cancer	3	**4.30**	**0.7**	**16**	**14.00**	**1.1**	**11**	**12.28**	**0.9**	**21**	**17.24**	**1.2**	**51**	**47.82**	**1.1**
Buccal cavity, pharynx	**0**	**0.06**	**0.0**	**1**	**0.20**	**5.0**	**1**	**0.17**	**5.7**	**1**	**0.25**	**4.1**	**3**	**0.68**	**4.4**
Lip	0	0.01	0.0	0	0.03	0.0	1	0.03	38.1	0	0.04	0.0	1	0.11	9.4
Tongue	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.13	0.0
Salivary gland	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.13	0.0
Gum, other mouth	0	0.02	0.0	0	0.06	0.0	0	0.05	0.0	0	0.08	0.0	0	0.21	0.0
Pharynx	0	0.01	0.0	1	0.03	30.4	0	0.03	0.0	1	0.04	26.7	2	0.11	18.5[b]
Digestive system	**0**	**1.66**	**0.0**	**6**	**5.48**	**1.1**	**5**	**4.87**	**1.0**	**8**	**6.78**	**1.2**	**19**	**18.80**	**1.0**
Esophagus	0	0.05	0.0	0	0.17	0.0	0	0.15	0.0	0	0.21	0.0	0	0.57	0.0
Stomach	0	0.48	0.0	3	1.56	1.9	1	1.36	0.7	4	1.67	2.4	8	5.07	1.6
Colon	0	0.49	0.0	2	1.64	1.2	3	1.48	2.0	3	2.21	1.4	8	5.83	1.4
Rectum	0	0.28	0.0	1	0.91	1.1	0	0.80	0.0	1	1.11	0.9	2	3.10	0.6
Liver, biliary	0	0.13	0.0	0	0.44	0.0	1	0.41	2.4	0	0.63	0.0	1	1.62	0.6
Pancreas	0	0.16	0.0	0	0.51	0.0	0	0.47	0.0	0	0.72	0.0	0	1.85	0.0
Respiratory system	**1**	**0.20**	**4.9**	**0**	**0.66**	**0.0**	**1**	**0.60**	**1.7**	**2**	**0.91**	**2.2**	**4**	**2.38**	**1.7**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Larynx	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Trachea, bronchus, lung	1	0.17	5.9	0	0.55	0.0	1	0.50	2.0	2	0.77	2.6	4	1.99	2.0
Female breast	1	0.85	1.2	4	2.73	1.5	1	2.38	0.4	4	3.34	1.2	10	9.30	1.1
Female genital tract	**1**	**0.71**	**1.4**	**3**	**2.26**	**1.3**	**2**	**1.89**	**1.1**	**3**	**2.53**	**1.2**	**9**	**7.39**	**1.2**
Cervix uteri	0	0.21	0.0	2	0.67	3.0	0	0.53	0.0	1	0.65	1.5	3	2.07	1.5
Corpus uteri	0	0.20	0.0	0	0.64	0.0	1	0.54	1.9	1	0.75	1.3	2	2.12	0.9
Uterus, NOS	0	0.02	0.0	0	0.07	0.0	0	0.06	0.0	0	0.08	0.0	0	0.24	0.0
Ovary, fallopian tubes	1	0.22	4.6	1	0.69	1.4	0	0.59	0.0	0	0.82	0.0	2	2.32	0.9
Kidney, renal pelvis, ureter	0	0.11	0.0	0	0.36	0.0	0	0.32	0.0	1	0.47	2.1	1	1.26	0.8
Bladder, other urinary	0	0.12	0.0	0	0.40	0.0	1	0.36	2.8	1	0.55	1.8	2	1.43	1.4
Melanoma of the skin	0	0.05	0.0	0	0.16	0.0	1	0.14	7.3	0	0.20	0.0	1	0.55	1.8
Eye	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0
Brain, central nervous system	0	0.07	0.0	1	0.21	4.7	0	0.18	0.0	0	0.26	0.0	1	0.72	1.4
Thyroid gland	0	0.03	0.0	0	0.10	0.0	0	0.09	0.0	0	0.13	0.0	0	0.34	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Connective tissue	0	0.01	0.0	0	0.05	0.0	0	0.04	0.0	0	0.05	0.0	0	0.14	0.0
Lymphatic, hematopoietic system	**0**	**0.22**	**0.0**	**1**	**0.74**	**1.4**	**0**	**0.66**	**0.0**	**1**	**0.99**	**1.0**	**2**	**2.61**	**0.8**
Non-Hodgkin's lymphoma	0	0.07	0.0	0	0.22	0.0	0	0.20	0.0	0	0.30	0.0	0	0.78	0.0
Hodgkin's disease	0	0.01	0.0	0	0.05	0.0	0	0.04	0.0	0	0.06	0.0	0	0.16	0.0
Multiple myeloma	0	0.04	0.0	0	0.15	0.0	0	0.13	0.0	1	0.20	4.9	1	0.53	1.9
Leukemias	0	0.10	0.0	1	0.31	3.2	0	0.28	0.0	0	0.42	0.0	1	1.12	0.9
Chronic lymphocytic	0	0.04	0.0	0	0.15	0.0	0	0.14	0.0	0	0.21	0.0	0	0.54	0.0
Acute nonlymphocytic	0	0.03	0.0	1	0.08	12.2	0	0.07	0.0	0	0.12	0.0	1	0.30	3.3

[a] ICD-7 code = 140.

[b] $P < .05$.

TONGUE
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the tongue, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	601	506	1,107
No. who developed a second primary cancer	43	25	68
Average age at diagnosis of first cancer, yr	64	69	66
Average yr of diagnosis of first cancer	1963	1963	1964
Person-yr of follow-up	2,396	2,372	4,768
Average follow-up, yr	4.0	4.7	4.3
Percent given radiotherapy for first cancer	74	67	71

[a] ICD-7 code = 141.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the tongue in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	59	86.8
Only the first cancer	7	10.3
Only the second cancer	1	1.5
Neither first nor second cancer	1	1.5
Total second primary cancers	68	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

TONGUE
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the tongue among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,107			691			294			151			1,107		
Person-yr in interval	905			1,659			1,068			1,136			4,768		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**7**	**9.81**	**0.7**	**29**	**18.12**	**1.6^b**	**11**	**12.87**	**0.9**	**21**	**16.80**	**1.3**	**68**	**57.59**	**1.2**
All excluding site of initial cancer	**7**	**9.78**	**0.7**	**29**	**18.07**	**1.6^b**	**11**	**12.83**	**0.9**	**21**	**16.76**	**1.3**	**68**	**57.44**	**1.2**
Buccal cavity, pharynx	**0**	**0.25**	**0.0**	**3**	**0.43**	**7.0^b**	**1**	**0.29**	**3.4**	**0**	**0.36**	**0.0**	**4**	**1.35**	**3.0**
Lip	0	0.11	0.0	0	0.19	0.0	0	0.12	0.0	0	0.16	0.0	0	0.58	0.0
Tongue	0	0.03	0.0	0	0.05	0.0	0	0.04	0.0	0	0.04	0.0	0	0.15	0.0
Salivary gland	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Gum, other mouth	0	0.04	0.0	2	0.07	28.6^b	1	0.06	16.7	0	0.08	0.0	3	0.25	12.0^b
Pharynx	0	0.04	0.0	1	0.07	14.3	0	0.05	0.0	0	0.06	0.0	1	0.21	4.8
Digestive system	**4**	**3.98**	**1.0**	**6**	**7.22**	**0.8**	**2**	**5.08**	**0.4**	**6**	**6.49**	**0.9**	**18**	**22.78**	**0.8**
Esophagus	0	0.17	0.0	1	0.28	3.6	0	0.19	0.0	2	0.24	8.3	3	0.88	3.4
Stomach	1	1.32	0.8	1	2.34	0.4	0	1.54	0.0	1	1.80	0.6	3	7.00	0.4
Colon	1	0.97	1.0	2	1.80	1.1	1	1.34	0.7	1	1.83	0.5	5	5.96	0.8
Rectum	0	0.78	0.0	0	1.40	0.0	0	0.98	0.0	0	1.24	0.0	0	4.41	0.0^b
Liver, biliary	1	0.23	4.3	1	0.45	2.2	0	0.35	0.0	0	0.49	0.0	2	1.52	1.3
Pancreas	1	0.35	2.9	0	0.65	0.0	1	0.50	2.0	1	0.69	1.4	3	2.18	1.4
Respiratory system	**1**	**1.18**	**0.8**	**6**	**2.16**	**2.8^b**	**4**	**1.52**	**2.6**	**6**	**2.17**	**2.8^b**	**17**	**7.03**	**2.4^b**
Nasal cavities, sinuses	0	0.03	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.12	0.0
Larynx	0	0.08	0.0	1	0.14	7.1	0	0.09	0.0	1	0.12	8.3	2	0.44	4.5
Trachea, bronchus, lung	1	1.00	1.0	5	1.86	2.7	4	1.30	3.1	5	1.89	2.6	15	6.05	2.5^b
Female breast	0	0.86	0.0	2	1.69	1.2	1	1.25	0.8	2	1.47	1.4	5	5.27	0.9
Female genital tract	**0**	**0.69**	**0.0**	**3**	**1.37**	**2.2**	**0**	**0.98**	**0.0**	**1**	**1.08**	**0.9**	**4**	**4.13**	**1.0**
Cervix uteri	0	0.20	0.0	1	0.39	2.5	0	0.27	0.0	0	0.27	0.0	1	1.14	0.9
Corpus uteri	0	0.20	0.0	0	0.39	0.0	0	0.28	0.0	0	0.32	0.0	0	1.19	0.0
Uterus, NOS	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.04	0.0	0	0.15	0.0
Ovary, fallopian tubes	0	0.21	0.0	1	0.42	2.4	0	0.31	0.0	0	0.35	0.0	1	1.29	0.8
Prostate gland	0	0.72	0.0	0	1.27	0.0	1	0.92	1.1	1	1.44	0.7	2	4.34	0.5
Testis	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Kidney, renal pelvis, ureter	1	0.28	3.6	3	0.52	5.8^b	1	0.37	2.7	0	0.51	0.0	5	1.68	3.0
Bladder, other urinary	0	0.52	0.0	3	0.96	3.1	0	0.68	0.0	4	1.00	4.0^b	7	3.18	2.2
Melanoma of the skin	0	0.09	0.0	0	0.17	0.0	0	0.12	0.0	1	0.16	6.3	1	0.54	1.9
Eye	0	0.03	0.0	0	0.05	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Brain, central nervous system	1	0.14	7.1	0	0.28	0.0	0	0.19	0.0	0	0.22	0.0	1	0.83	1.2
Thyroid gland	0	0.04	0.0	1	0.09	11.1	0	0.07	0.0	0	0.09	0.0	1	0.28	3.6
Bone	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.10	0.0
Connective tissue	0	0.03	0.0	1	0.07	14.3	0	0.04	0.0	0	0.05	0.0	1	0.18	5.6
Lymphatic, hematopoietic system	**0**	**0.55**	**0.0**	**1**	**1.03**	**1.0**	**0**	**0.76**	**0.0**	**0**	**1.03**	**0.0**	**1**	**3.38**	**0.3**
Non-Hodgkin's lymphoma	0	0.16	0.0	0	0.28	0.0	0	0.21	0.0	0	0.28	0.0	0	0.92	0.0
Hodgkin's disease	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Multiple myeloma	0	0.10	0.0	0	0.20	0.0	0	0.15	0.0	0	0.20	0.0	0	0.65	0.0
Leukemias	0	0.26	0.0	1	0.47	2.1	0	0.35	0.0	0	0.48	0.0	1	1.56	0.6
Chronic lymphocytic	0	0.14	0.0	1	0.25	4.0	0	0.19	0.0	0	0.26	0.0	1	0.84	1.2
Acute nonlymphocytic	0	0.05	0.0	0	0.10	0.0	0	0.08	0.0	0	0.12	0.0	0	0.37	0.0

[a] ICD-7 code = 141.

[b] $P < .05$.

TONGUE
MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the tongue among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	601			365			144			74			601		
Person-yr in interval	489			846			514			547			2,396		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**5.33**	**0.7**	**14**	**9.34**	**1.5**	**8**	**6.35**	**1.3**	**17**	**9.09**	**1.9**[b]	**43**	**30.11**	**1.4**[b]
All excluding site of initial cancer	**4**	**5.31**	**0.8**	**14**	**9.32**	**1.5**	**8**	**6.33**	**1.3**	**17**	**9.07**	**1.9**[b]	**43**	**30.04**	**1.4**[b]
Buccal cavity, pharynx	**0**	**0.18**	**0.0**	**2**	**0.31**	**6.4**	**0**	**0.20**	**0.0**	**0**	**0.25**	**0.0**	**2**	**0.95**	**2.1**
Lip	0	0.10	0.0	0	0.17	0.0	0	0.11	0.0	0	0.14	0.0	0	0.52	0.0
Tongue	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Gum, other mouth	0	0.02	0.0	1	0.04	24.1	0	0.03	0.0	0	0.04	0.0	1	0.13	7.6
Pharynx	0	0.03	0.0	1	0.05	20.3	0	0.03	0.0	0	0.04	0.0	1	0.15	6.9
Digestive system	**3**	**2.17**	**1.4**	**3**	**3.70**	**0.8**	**2**	**2.48**	**0.8**	**6**	**3.38**	**1.8**	**14**	**11.73**	**1.2**
Esophagus	0	0.11	0.0	1	0.17	5.7	0	0.11	0.0	2	0.14	14.4[b]	3	0.53	5.7[b]
Stomach	1	0.75	1.3	0	1.25	0.0	0	0.82	0.0	1	1.00	1.0	2	3.81	0.5
Colon	0	0.46	0.0	2	0.80	2.5	1	0.55	1.8	1	0.84	1.2	4	2.66	1.5
Rectum	0	0.48	0.0	0	0.82	0.0	0	0.55	0.0	0	0.74	0.0	0	2.60	0.0
Liver, biliary	1	0.10	10.0	0	0.18	0.0	0	0.13	0.0	0	0.21	0.0	1	0.62	1.6
Pancreas	1	0.20	5.1	0	0.35	0.0	1	0.25	4.1	1	0.37	2.7	3	1.16	2.6
Respiratory system	**0**	**0.98**	**0.0**	**4**	**1.76**	**2.3**	**3**	**1.20**	**2.5**	**6**	**1.78**	**3.4**[b]	**13**	**5.72**	**2.3**[b]
Nasal cavities, sinuses	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Larynx	0	0.07	0.0	1	0.12	8.1	0	0.08	0.0	1	0.11	8.9	2	0.39	5.1
Trachea, bronchus, lung	0	0.84	0.0	3	1.53	2.0	3	1.04	2.9	5	1.56	3.2[b]	11	4.97	2.2[b]
Prostate gland	0	0.72	0.0	0	1.27	0.0	1	0.92	1.1	1	1.44	0.7	2	4.34	0.5
Testis	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Kidney, renal pelvis, ureter	0	0.17	0.0	3	0.30	10.1[b]	1	0.20	5.0	0	0.30	0.0	4	0.96	4.2[b]
Bladder, other urinary	0	0.40	0.0	2	0.72	2.8	0	0.49	0.0	4	0.76	5.3[b]	6	2.38	2.5
Melanoma of the skin	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	0	0.07	0.0	0	0.24	0.0
Eye	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Brain, central nervous system	1	0.08	12.0	0	0.15	0.0	0	0.10	0.0	0	0.11	0.0	1	0.44	2.3
Thyroid gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Connective tissue	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.10	0.0
Lymphatic, hematopoietic system	**0**	**0.33**	**0.0**	**0**	**0.59**	**0.0**	**0**	**0.41**	**0.0**	**0**	**0.59**	**0.0**	**0**	**1.93**	**0.0**
Non-Hodgkin's lymphoma	0	0.09	0.0	0	0.15	0.0	0	0.10	0.0	0	0.15	0.0	0	0.49	0.0
Hodgkin's disease	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Multiple myeloma	0	0.06	0.0	0	0.11	0.0	0	0.08	0.0	0	0.11	0.0	0	0.36	0.0
Leukemias	0	0.16	0.0	0	0.28	0.0	0	0.20	0.0	0	0.29	0.0	0	0.93	0.0
Chronic lymphocytic	0	0.09	0.0	0	0.16	0.0	0	0.11	0.0	0	0.16	0.0	0	0.53	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.07	0.0	0	0.21	0.0

[a] ICD-7 code = 141.

[b] $P < .05$.

TONGUE
FEMALES

TABLE 2E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the tongue among females in Denmark, 1943-80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	506			326			150			77			506		
Person-yr in interval	416			813			554			589			2,372		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**3**	**4.48**	**0.7**	**15**	**8.78**	**1.7**	**3**	**6.52**	**0.5**	**4**	**7.71**	**0.5**	**25**	**27.48**	**0.9**
All excluding site of initial cancer	**3**	**4.47**	**0.7**	**15**	**8.75**	**1.7**	**3**	**6.50**	**0.5**	**4**	**7.69**	**0.5**	**25**	**27.40**	**0.9**
Buccal cavity, pharynx	**0**	**0.07**	**0.0**	**1**	**0.12**	**8.0**	**1**	**0.09**	**10.6**	**0**	**0.11**	**0.0**	**2**	**0.40**	**5.0**
Lip	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Tongue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Gum, other mouth	0	0.02	0.0	1	0.03	28.8	1	0.03	35.6	0	0.04	0.0	2	0.12	16.9[b]
Pharynx	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.06	0.0
Digestive system	**1**	**1.81**	**0.6**	**3**	**3.52**	**0.9**	**0**	**2.60**	**0.0**	**0**	**3.11**	**0.0**	**4**	**11.05**	**0.4**[b]
Esophagus	0	0.06	0.0	0	0.11	0.0	0	0.08	0.0	0	0.10	0.0	0	0.35	0.0
Stomach	0	0.57	0.0	1	1.09	0.9	0	0.72	0.0	0	0.80	0.0	1	3.19	0.3
Colon	1	0.51	2.0	0	1.00	0.0	0	0.79	0.0	0	0.99	0.0	1	3.30	0.3
Rectum	0	0.30	0.0	0	0.58	0.0	0	0.43	0.0	0	0.50	0.0	0	1.81	0.0
Liver, biliary	0	0.13	0.0	1	0.27	3.7	0	0.22	0.0	0	0.28	0.0	1	0.90	1.1
Pancreas	0	0.15	0.0	0	0.30	0.0	0	0.25	0.0	0	0.32	0.0	0	1.02	0.0
Respiratory system	**1**	**0.20**	**5.0**	**2**	**0.40**	**5.0**	**1**	**0.32**	**3.2**	**0**	**0.39**	**0.0**	**4**	**1.31**	**3.1**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Trachea, bronchus, lung	1	0.16	6.1	2	0.33	6.1	1	0.26	3.8	0	0.33	0.0	4	1.08	3.7
Female breast	0	0.86	0.0	2	1.69	1.2	1	1.25	0.8	2	1.47	1.4	5	5.27	0.9
Female genital tract	**0**	**0.69**	**0.0**	**3**	**1.37**	**2.2**	**0**	**0.98**	**0.0**	**1**	**1.08**	**0.9**	**4**	**4.13**	**1.0**
Cervix uteri	0	0.20	0.0	1	0.39	2.5	0	0.27	0.0	0	0.27	0.0	1	1.14	0.9
Corpus uteri	0	0.20	0.0	0	0.39	0.0	0	0.28	0.0	0	0.32	0.0	0	1.19	0.0
Uterus, NOS	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.04	0.0	0	0.15	0.0
Ovary, fallopian tubes	0	0.21	0.0	1	0.42	2.4	0	0.31	0.0	0	0.35	0.0	1	1.29	0.8
Kidney, renal pelvis, ureter	1	0.11	9.0	0	0.22	0.0	0	0.17	0.0	0	0.21	0.0	1	0.72	1.4
Bladder, other urinary	0	0.12	0.0	1	0.24	4.2	0	0.19	0.0	0	0.24	0.0	1	0.80	1.3
Melanoma of the skin	0	0.05	0.0	0	0.09	0.0	0	0.07	0.0	1	0.09	11.3	1	0.30	3.4
Eye	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Brain, central nervous system	0	0.06	0.0	0	0.13	0.0	0	0.09	0.0	0	0.11	0.0	0	0.39	0.0
Thyroid gland	0	0.03	0.0	1	0.06	16.5	0	0.05	0.0	0	0.06	0.0	1	0.19	5.1
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.01	0.0	1	0.03	34.8	0	0.02	0.0	0	0.02	0.0	1	0.08	12.1
Lymphatic, hematopoietic system	**0**	**0.22**	**0.0**	**1**	**0.44**	**2.3**	**0**	**0.35**	**0.0**	**0**	**0.44**	**0.0**	**1**	**1.45**	**0.7**
Non-Hodgkin's lymphoma	0	0.07	0.0	0	0.13	0.0	0	0.11	0.0	0	0.13	0.0	0	0.43	0.0
Hodgkin's disease	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Multiple myeloma	0	0.04	0.0	0	0.09	0.0	0	0.07	0.0	0	0.09	0.0	0	0.29	0.0
Leukemias	0	0.10	0.0	1	0.19	5.3	0	0.15	0.0	0	0.19	0.0	1	0.63	1.6
Chronic lymphocytic	0	0.05	0.0	1	0.09	10.8	0	0.08	0.0	0	0.10	0.0	1	0.31	3.2
Acute nonlymphocytic	0	0.02	0.0	0	0.04	0.0	0	0.04	0.0	0	0.05	0.0	0	0.16	0.0

[a] ICD-7 code = 141.

[b] $P < .05$.

SALIVARY GLAND
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the salivary gland, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	823	930	1,753
No. who developed a second primary cancer	61	88	149
Average age at diagnosis of first cancer, yr	57	55	56
Average yr of diagnosis of first cancer	1962	1961	1961
Person-yr of follow-up	7,696	11,504	19,200
Average follow-up, yr	9.4	12.4	11.2
Percent given radiotherapy for first cancer	69	62	66

[a] ICD-7 code = 142.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the salivary gland in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	88	59.1
Only the first cancer	15	10.1
Only the second cancer	36	24.2
Neither first nor second cancer	10	6.7
Total second primary cancers	149	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

SALIVARY GLAND
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the salivary gland among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,753			1,513			1,095			806			1,753		
Person-yr in interval	1,636			4,971			4,718			7,874			19,200		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8**	**12.12**	**0.7**	**45**	**34.95**	**1.3**	**34**	**35.22**	**1.0**	**62**	**70.31**	**0.9**	**149**	**152.61**	**1.0**
All excluding site of initial cancer	**8**	**12.08**	**0.7**	**44**	**34.83**	**1.3**	**34**	**35.11**	**1.0**	**62**	**70.14**	**0.9**	**148**	**152.17**	**1.0**
Buccal cavity, pharynx	**1**	**0.29**	**3.4**	**3**	**0.79**	**3.8**	**0**	**0.75**	**0.0**	**0**	**1.43**	**0.0**	**4**	**3.27**	**1.2**
Lip	0	0.13	0.0	1	0.34	2.9	0	0.30	0.0	0	0.55	0.0	1	1.32	0.8
Tongue	1	0.03	33.3	1	0.08	12.5	0	0.08	0.0	0	0.16	0.0	2	0.34	5.9
Salivary gland	0	0.04	0.0	1	0.12	8.3	0	0.11	0.0	0	0.17	0.0	1	0.44	2.3
Gum, other mouth	0	0.05	0.0	0	0.13	0.0	0	0.13	0.0	0	0.31	0.0	0	0.62	0.0
Pharynx	0	0.04	0.0	0	0.13	0.0	0	0.12	0.0	0	0.25	0.0	0	0.54	0.0
Digestive system	**2**	**4.45**	**0.4**	**14**	**12.35**	**1.1**	**8**	**12.08**	**0.7**	**12**	**22.97**	**0.5**[b]	**36**	**51.85**	**0.7**[b]
Esophagus	0	0.17	0.0	2	0.45	4.4	0	0.42	0.0	1	0.77	1.3	3	1.80	1.7
Stomach	0	1.40	0.0	1	3.71	0.3	3	3.32	0.9	1	5.24	0.2	5	13.68	0.4[b]
Colon	0	1.11	0.0	4	3.22	1.2	1	3.36	0.3	3	7.02	0.4	8	14.72	0.5
Rectum	1	0.90	1.1	4	2.49	1.6	2	2.40	0.8	1	4.51	0.2	8	10.29	0.8
Liver, biliary	0	0.27	0.0	2	0.83	2.4	1	0.90	1.1	4	1.95	2.1	7	3.96	1.8
Pancreas	1	0.42	2.4	1	1.20	0.8	1	1.27	0.8	2	2.74	0.7	5	5.62	0.9
Respiratory system	**1**	**1.45**	**0.7**	**7**	**4.00**	**1.8**	**2**	**4.05**	**0.5**	**13**	**9.17**	**1.4**	**23**	**18.66**	**1.2**
Nasal cavities, sinuses	0	0.03	0.0	1	0.08	12.5	0	0.07	0.0	1	0.14	7.1	2	0.32	6.3
Larynx	0	0.09	0.0	1	0.26	3.8	0	0.25	0.0	0	0.57	0.0	1	1.17	0.9
Trachea, bronchus, lung	1	1.25	0.8	5	3.44	1.5	2	3.50	0.6	11	8.03	1.4	19	16.22	1.2
Female breast	1	1.22	0.8	4	4.08	1.0	6	4.41	1.4	13	9.07	1.4	24	18.78	1.3
Female genital tract	**1**	**1.21**	**0.8**	**6**	**4.05**	**1.5**	**4**	**4.23**	**0.9**	**8**	**7.98**	**1.0**	**19**	**17.47**	**1.1**
Cervix uteri	0	0.46	0.0	2	1.57	1.3	2	1.57	1.3	0	2.59	0.0	4	6.19	0.6
Corpus uteri	0	0.31	0.0	1	1.03	1.0	0	1.12	0.0	2	2.33	0.9	3	4.78	0.6
Uterus, NOS	0	0.03	0.0	0	0.09	0.0	0	0.08	0.0	1	0.13	7.5	1	0.34	3.0
Ovary, fallopian tubes	1	0.34	3.0	2	1.13	1.8	2	1.21	1.6	4	2.43	1.6	9	5.11	1.8
Prostate gland	0	0.82	0.0	2	1.99	1.0	5	1.89	2.6	1	3.67	0.3	8	8.37	1.0
Testis	0	0.04	0.0	0	0.11	0.0	0	0.11	0.0	0	0.19	0.0	0	0.46	0.0
Kidney, renal pelvis, ureter	1	0.34	2.9	0	0.99	0.0	2	1.02	2.0	3	2.15	1.4	6	4.51	1.3
Bladder, other urinary	0	0.62	0.0	2	1.70	1.2	2	1.74	1.1	3	3.86	0.8	7	7.92	0.9
Melanoma of the skin	0	0.12	0.0	1	0.40	2.5	1	0.45	2.2	0	1.00	0.0	2	1.99	1.0
Eye	0	0.04	0.0	0	0.11	0.0	0	0.11	0.0	1	0.20	5.0	1	0.45	2.2
Brain, central nervous system	1	0.23	4.3	1	0.70	1.4	1	0.72	1.4	2	1.43	1.4	5	3.08	1.6
Thyroid gland	0	0.06	0.0	1	0.18	5.6	0	0.19	0.0	3	0.38	7.9[b]	4	0.80	5.0[b]
Bone	0	0.02	0.0	0	0.08	0.0	1	0.07	14.3	0	0.11	0.0	1	0.28	3.6
Connective tissue	0	0.04	0.0	0	0.13	0.0	0	0.13	0.0	0	0.21	0.0	0	0.51	0.0
Lymphatic, hematopoietic system	**0**	**0.70**	**0.0**	**3**	**2.05**	**1.5**	**0**	**2.10**	**0.0**	**1**	**4.24**	**0.2**	**4**	**9.10**	**0.4**
Non-Hodgkin's lymphoma	0	0.19	0.0	2	0.55	3.6	0	0.58	0.0	1	1.23	0.8	3	2.56	1.2
Hodgkin's disease	0	0.07	0.0	0	0.19	0.0	0	0.18	0.0	0	0.32	0.0	0	0.75	0.0
Multiple myeloma	0	0.13	0.0	0	0.38	0.0	0	0.40	0.0	0	0.82	0.0	0	1.73	0.0
Leukemias	0	0.31	0.0	1	0.90	1.1	0	0.92	0.0	0	1.83	0.0	1	3.97	0.3
Chronic lymphocytic	0	0.16	0.0	0	0.45	0.0	0	0.45	0.0	0	0.86	0.0	0	1.92	0.0
Acute nonlymphocytic	0	0.07	0.0	0	0.22	0.0	0	0.25	0.0	0	0.57	0.0	0	1.13	0.0

[a] ICD-7 code = 142.

[b] $P < .05$.

SALIVARY GLAND
MALES

TABLE 3D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the salivary gland among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	823			673			440			317			823		
Person-yr in interval	752			2,055			1,847			3,041			7,696		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**3**	**6.27**	**0.5**	**21**	**15.66**	**1.3**	**12**	**14.57**	**0.8**	**25**	**28.54**	**0.9**	**61**	**65.05**	**0.9**
All excluding site of initial cancer	**3**	**6.25**	**0.5**	**20**	**15.61**	**1.3**	**12**	**14.53**	**0.8**	**25**	**28.47**	**0.9**	**60**	**64.87**	**0.9**
Buccal cavity, pharynx	**0**	**0.21**	**0.0**	**2**	**0.53**	**3.8**	**0**	**0.48**	**0.0**	**0**	**0.89**	**0.0**	**2**	**2.12**	**0.9**
Lip	0	0.12	0.0	1	0.30	3.4	0	0.26	0.0	0	0.47	0.0	1	1.15	0.9
Tongue	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.07	0.0	0	0.15	0.0
Salivary gland	0	0.02	0.0	1	0.05	20.5	0	0.04	0.0	0	0.07	0.0	1	0.18	5.4
Gum, other mouth	0	0.03	0.0	0	0.07	0.0	0	0.06	0.0	0	0.13	0.0	0	0.29	0.0
Pharynx	0	0.03	0.0	0	0.08	0.0	0	0.07	0.0	0	0.15	0.0	0	0.34	0.0
Digestive system	**1**	**2.45**	**0.4**	**7**	**5.94**	**1.2**	**2**	**5.33**	**0.4**	**6**	**9.46**	**0.6**	**16**	**23.18**	**0.7**
Esophagus	0	0.11	0.0	1	0.27	3.8	0	0.23	0.0	1	0.40	2.5	2	1.01	2.0
Stomach	0	0.82	0.0	0	1.95	0.0	1	1.66	0.6	0	2.49	0.0	1	6.92	0.1[b]
Colon	0	0.53	0.0	3	1.30	2.3	0	1.22	0.0	2	2.37	0.8	5	5.42	0.9
Rectum	1	0.55	1.8	1	1.34	0.7	1	1.20	0.8	0	2.13	0.0	3	5.21	0.6
Liver, biliary	0	0.12	0.0	1	0.31	3.3	0	0.30	0.0	2	0.62	3.2	3	1.35	2.2
Pancreas	0	0.24	0.0	1	0.60	1.7	0	0.57	0.0	1	1.16	0.9	2	2.56	0.8
Respiratory system	**0**	**1.20**	**0.0**	**4**	**3.13**	**1.3**	**1**	**3.02**	**0.3**	**11**	**6.71**	**1.6**	**16**	**14.05**	**1.1**
Nasal cavities, sinuses	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	1	0.08	12.5	1	0.19	5.4
Larynx	0	0.08	0.0	1	0.22	4.6	0	0.21	0.0	0	0.47	0.0	1	0.98	1.0
Trachea, bronchus, lung	0	1.04	0.0	3	2.72	1.1	1	2.63	0.4	9	5.90	1.5	13	12.29	1.1
Prostate gland	0	0.82	0.0	2	1.99	1.0	5	1.89	2.6	1	3.67	0.3	8	8.37	1.0
Testis	0	0.04	0.0	0	0.11	0.0	0	0.11	0.0	0	0.19	0.0	0	0.46	0.0
Kidney, renal pelvis, ureter	1	0.20	5.0	0	0.51	0.0	1	0.49	2.0	2	1.01	2.0	4	2.21	1.8
Bladder, other urinary	0	0.48	0.0	1	1.22	0.8	1	1.18	0.9	3	2.60	1.2	5	5.48	0.9
Melanoma of the skin	0	0.05	0.0	0	0.14	0.0	0	0.14	0.0	0	0.32	0.0	0	0.66	0.0
Eye	0	0.02	0.0	0	0.05	0.0	0	0.05	0.0	0	0.09	0.0	0	0.21	0.0
Brain, central nervous system	1	0.11	8.7	1	0.31	3.2	1	0.29	3.4	1	0.58	1.7	4	1.29	3.1
Thyroid gland	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.09	0.0	0	0.19	0.0
Bone	0	0.01	0.0	0	0.04	0.0	1	0.03	31.1	0	0.05	0.0	1	0.13	7.7
Connective tissue	0	0.02	0.0	0	0.06	0.0	0	0.06	0.0	0	0.09	0.0	0	0.23	0.0
Lymphatic, hematopoietic system	**0**	**0.41**	**0.0**	**3**	**1.06**	**2.8**	**0**	**1.00**	**0.0**	**1**	**1.93**	**0.5**	**4**	**4.41**	**0.9**
Non-Hodgkin's lymphoma	0	0.11	0.0	2	0.27	7.3	0	0.26	0.0	1	0.52	1.9	3	1.16	2.6
Hodgkin's disease	0	0.04	0.0	0	0.10	0.0	0	0.09	0.0	0	0.16	0.0	0	0.38	0.0
Multiple myeloma	0	0.07	0.0	0	0.19	0.0	0	0.18	0.0	0	0.36	0.0	0	0.80	0.0
Leukemias	0	0.19	0.0	1	0.49	2.0	0	0.46	0.0	0	0.87	0.0	1	2.02	0.5
Chronic lymphocytic	0	0.11	0.0	0	0.27	0.0	0	0.25	0.0	0	0.45	0.0	0	1.08	0.0
Acute nonlymphocytic	0	0.04	0.0	0	0.11	0.0	0	0.11	0.0	0	0.25	0.0	0	0.52	0.0

[a] ICD-7 code = 142.

[b] $P < .05$.

SALIVARY GLAND
FEMALES

TABLE 3E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the salivary gland among females in Denmark, 1943-80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	930			840			655			489			930		
Person-yr in interval	884			2,916			2,871			4,833			11,504		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**5**	**5.85**	**0.9**	**24**	**19.29**	**1.2**	**22**	**20.65**	**1.1**	**37**	**41.77**	**0.9**	**88**	**87.56**	**1.0**
All excluding site of initial cancer	**5**	**5.83**	**0.9**	**24**	**19.22**	**1.2**	**22**	**20.58**	**1.1**	**37**	**41.67**	**0.9**	**88**	**87.30**	**1.0**
Buccal cavity, pharynx	**1**	**0.08**	**12.4**	**1**	**0.26**	**3.9**	**0**	**0.27**	**0.0**	**0**	**0.54**	**0.0**	**2**	**1.15**	**1.7**
Lip	0	0.01	0.0	0	0.04	0.0	0	0.04	0.0	0	0.08	0.0	0	0.17	0.0
Tongue	1	0.01	71.6[b]	1	0.04	23.4	0	0.05	0.0	0	0.09	0.0	2	0.19	10.3[b]
Salivary gland	0	0.02	0.0	0	0.07	0.0	0	0.07	0.0	0	0.10	0.0	0	0.26	0.0
Gum, other mouth	0	0.02	0.0	0	0.06	0.0	0	0.07	0.0	0	0.18	0.0	0	0.33	0.0
Pharynx	0	0.01	0.0	0	0.05	0.0	0	0.05	0.0	0	0.10	0.0	0	0.20	0.0
Digestive system	**1**	**2.00**	**0.5**	**7**	**6.41**	**1.1**	**6**	**6.75**	**0.9**	**6**	**13.51**	**0.4**[b]	**20**	**28.67**	**0.7**
Esophagus	0	0.06	0.0	1	0.18	5.5	0	0.19	0.0	0	0.37	0.0	1	0.79	1.3
Stomach	0	0.58	0.0	1	1.76	0.6	2	1.66	1.2	1	2.75	0.4	4	6.76	0.6
Colon	0	0.58	0.0	1	1.92	0.5	1	2.14	0.5	1	4.65	0.2	3	9.30	0.3[b]
Rectum	0	0.35	0.0	3	1.15	2.6	1	1.20	0.8	1	2.38	0.4	5	5.08	1.0
Liver, biliary	0	0.15	0.0	1	0.52	1.9	1	0.60	1.7	2	1.33	1.5	4	2.61	1.5
Pancreas	1	0.18	5.6	0	0.60	0.0	1	0.70	1.4	1	1.58	0.6	3	3.06	1.0
Respiratory system	**1**	**0.25**	**3.9**	**3**	**0.87**	**3.5**	**1**	**1.03**	**1.0**	**2**	**2.46**	**0.8**	**7**	**4.61**	**1.5**
Nasal cavities, sinuses	0	0.01	0.0	1	0.03	35.3	0	0.03	0.0	0	0.06	0.0	1	0.13	7.8
Larynx	0	0.01	0.0	0	0.04	0.0	0	0.04	0.0	0	0.10	0.0	0	0.19	0.0
Trachea, bronchus, lung	1	0.21	4.8	2	0.72	2.8	1	0.87	1.2	2	2.13	0.9	6	3.93	1.5
Female breast	1	1.22	0.8	4	4.08	1.0	6	4.41	1.4	13	9.07	1.4	24	18.78	1.3
Female genital tract	**1**	**1.21**	**0.8**	**6**	**4.05**	**1.5**	**4**	**4.23**	**0.9**	**8**	**7.98**	**1.0**	**19**	**17.47**	**1.1**
Cervix uteri	0	0.46	0.0	2	1.57	1.3	2	1.57	1.3	0	2.59	0.0	4	6.19	0.6
Corpus uteri	0	0.31	0.0	1	1.03	1.0	0	1.12	0.0	2	2.33	0.9	3	4.78	0.6
Uterus, NOS	0	0.03	0.0	0	0.09	0.0	0	0.08	0.0	1	0.13	7.5	1	0.34	3.0
Ovary, fallopian tubes	1	0.34	3.0	2	1.13	1.8	2	1.21	1.6	4	2.43	1.6	9	5.11	1.8
Kidney, renal pelvis, ureter	0	0.14	0.0	0	0.48	0.0	1	0.53	1.9	1	1.14	0.9	2	2.30	0.9
Bladder, other urinary	0	0.14	0.0	1	0.48	2.1	1	0.56	1.8	0	1.26	0.0	2	2.44	0.8
Melanoma of the skin	0	0.07	0.0	1	0.26	3.8	1	0.31	3.2	0	0.68	0.0	2	1.33	1.5
Eye	0	0.02	0.0	0	0.06	0.0	0	0.06	0.0	1	0.11	9.2	1	0.24	4.1
Brain, central nervous system	0	0.12	0.0	0	0.39	0.0	0	0.43	0.0	1	0.85	1.2	1	1.79	0.6
Thyroid gland	0	0.04	0.0	1	0.13	7.5	0	0.15	0.0	3	0.29	10.4[b]	4	0.61	6.6[b]
Bone	0	0.01	0.0	0	0.04	0.0	0	0.04	0.0	0	0.06	0.0	0	0.15	0.0
Connective tissue	0	0.02	0.0	0	0.07	0.0	0	0.07	0.0	0	0.12	0.0	0	0.28	0.0
Lymphatic, hematopoietic system	**0**	**0.29**	**0.0**	**0**	**0.99**	**0.0**	**0**	**1.10**	**0.0**	**0**	**2.31**	**0.0**	**0**	**4.69**	**0.0**[b]
Non-Hodgkin's lymphoma	0	0.08	0.0	0	0.28	0.0	0	0.32	0.0	0	0.71	0.0	0	1.40	0.0
Hodgkin's disease	0	0.03	0.0	0	0.09	0.0	0	0.09	0.0	0	0.16	0.0	0	0.37	0.0
Multiple myeloma	0	0.06	0.0	0	0.19	0.0	0	0.22	0.0	0	0.46	0.0	0	0.93	0.0
Leukemias	0	0.12	0.0	0	0.41	0.0	0	0.46	0.0	0	0.96	0.0	0	1.95	0.0
Chronic lymphocytic	0	0.05	0.0	0	0.18	0.0	0	0.20	0.0	0	0.41	0.0	0	0.84	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.11	0.0	0	0.14	0.0	0	0.32	0.0	0	0.61	0.0

[a] ICD-7 code = 142.

[b] $P < .05$.

MOUTH
BOTH SEXES

TABLE 4A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the gum or other mouth, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,035	729	1,764
No. who developed a second primary cancer	90	41	131
Average age at diagnosis of first cancer, yr	66	68	67
Average yr of diagnosis of first cancer	1965	1967	1966
Person-yr of follow-up	4,715	3,462	8,177
Average follow-up, yr	4.6	4.8	4.7
Percent given radiotherapy for first cancer	77	75	76

[a] ICD-7 codes = 143–144.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the gum or other mouth in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	101	77.1
Only the first cancer	23	17.6
Only the second cancer	6	4.6
Neither first nor second cancer	1	0.8
Total second primary cancers	131	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

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TABLE 4C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the gum or other mouth among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval Person-yr in interval	1,764 1,525			1,239 3,013			531 1,864			247 1,775			1,764 8,177		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**17**	**17.84**	**1.0**	**51**	**35.20**	**1.4**^{b}	**39**	**23.09**	**1.7**^{b}	**24**	**23.98**	**1.0**	**131**	**100.11**	**1.3**^{b}
All excluding site of initial cancer	**17**	**17.76**	**1.0**	**51**	**35.04**	**1.5**^{b}	**39**	**22.99**	**1.7**^{b}	**22**	**23.87**	**0.9**	**129**	**99.66**	**1.3**^{b}
Buccal cavity, pharynx	**1**	**0.46**	**2.2**	**5**	**0.88**	**5.7**^{b}	**3**	**0.56**	**5.4**^{b}	**6**	**0.55**	**10.9**^{b}	**15**	**2.45**	**6.1**^{b}
Lip	1	0.20	5.0	4	0.40	10.0^{b}	1	0.26	3.8	1	0.25	4.0	7	1.12	6.3^{b}
Tongue	0	0.05	0.0	1	0.08	12.5	2	0.05	40.0^{b}	2	0.05	40.0^{b}	5	0.24	20.8^{b}
Salivary gland	0	0.05	0.0	0	0.10	0.0	0	0.06	0.0	0	0.06	0.0	0	0.26	0.0
Gum, other mouth	0	0.08	0.0	0	0.16	0.0	0	0.10	0.0	2	0.11	18.2^{b}	2	0.45	4.4
Pharynx	0	0.08	0.0	0	0.14	0.0	0	0.09	0.0	1	0.09	11.1	1	0.39	2.6
Digestive system	**7**	**6.99**	**1.0**	**20**	**13.53**	**1.5**	**14**	**8.87**	**1.6**	**6**	**8.94**	**0.7**	**47**	**38.33**	**1.2**
Esophagus	1	0.29	3.4	4	0.54	7.4^{b}	2	0.34	5.9	1	0.33	3.0	8	1.50	5.3^{b}
Stomach	3	2.16	1.4	5	4.06	1.2	2	2.63	0.8	2	2.43	0.8	12	11.29	1.1
Colon	2	1.78	1.1	8	3.51	2.3	4	2.33	1.7	1	2.49	0.4	15	10.10	1.5
Rectum	1	1.40	0.7	1	2.73	0.4	2	1.78	1.1	2	1.78	1.1	6	7.67	0.8
Liver, biliary	0	0.44	0.0	1	0.88	1.1	2	0.60	3.3	0	0.65	0.0	3	2.57	1.2
Pancreas	0	0.67	0.0	1	1.35	0.7	1	0.90	1.1	0	0.98	0.0	2	3.90	0.5
Respiratory system	**5**	**2.43**	**2.1**	**14**	**4.89**	**2.9**^{b}	**13**	**3.19**	**4.1**^{b}	**2**	**3.52**	**0.6**	**34**	**14.03**	**2.4**^{b}
Nasal cavities, sinuses	1	0.04	25.0	1	0.08	12.5	0	0.05	0.0	0	0.05	0.0	2	0.23	8.7
Larynx	0	0.16	0.0	1	0.32	3.1	0	0.20	0.0	0	0.22	0.0	1	0.89	1.1
Trachea, bronchus, lung	4	2.10	1.9	12	4.24	2.8^{b}	11	2.77	4.0^{b}	2	3.07	0.7	29	12.18	2.4^{b}
Female breast	0	1.34	0.0	1	2.64	0.4	0	1.66	0.0	2	1.72	1.2	3	7.35	0.4
Female genital tract	**1**	**1.07**	**0.9**	**3**	**2.18**	**1.4**	**1**	**1.34**	**0.7**	**1**	**1.33**	**0.8**	**6**	**5.93**	**1.0**
Cervix uteri	1	0.30	3.4	0	0.61	0.0	1	0.38	2.7	0	0.37	0.0	2	1.65	1.2
Corpus uteri	0	0.32	0.0	1	0.65	1.5	0	0.39	0.0	0	0.38	0.0	1	1.74	0.6
Uterus, NOS	0	0.04	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.18	0.0
Ovary, fallopian tubes	0	0.33	0.0	2	0.68	2.9	0	0.42	0.0	1	0.42	2.4	3	1.86	1.6
Prostate gland	1	1.52	0.7	0	3.10	0.0	0	2.20	0.0	3	2.35	1.3	4	9.18	0.4
Testis	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.20	0.0
Kidney, renal pelvis, ureter	0	0.53	0.0	1	1.05	1.0	0	0.69	0.0	0	0.74	0.0	1	3.01	0.3
Bladder, other urinary	2	1.07	1.9	3	2.15	1.4	1	1.44	0.7	2	1.57	1.3	8	6.24	1.3
Melanoma of the skin	0	0.17	0.0	0	0.34	0.0	1	0.22	4.5	1	0.23	4.3	2	0.95	2.1
Eye	0	0.05	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.27	0.0
Brain, central nervous system	0	0.27	0.0	1	0.54	1.9	0	0.34	0.0	1	0.35	2.9	2	1.49	1.3
Thyroid gland	0	0.08	0.0	0	0.15	0.0	0	0.10	0.0	0	0.10	0.0	0	0.44	0.0
Bone	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.03	0.0	0	0.17	0.0
Connective tissue	0	0.06	0.0	0	0.12	0.0	0	0.08	0.0	0	0.07	0.0	0	0.32	0.0
Lymphatic, hematopoietic system	**0**	**1.05**	**0.0**	**2**	**2.11**	**0.9**	**2**	**1.40**	**1.4**	**0**	**1.50**	**0.0**	**4**	**6.07**	**0.7**
Non-Hodgkin's lymphoma	0	0.29	0.0	0	0.57	0.0	2	0.38	5.3	0	0.40	0.0	2	1.64	1.2
Hodgkin's disease	0	0.07	0.0	1	0.14	7.1	0	0.09	0.0	0	0.09	0.0	1	0.39	2.6
Multiple myeloma	0	0.20	0.0	1	0.41	2.4	0	0.28	0.0	0	0.29	0.0	1	1.17	0.9
Leukemias	0	0.49	0.0	0	0.97	0.0	0	0.65	0.0	0	0.69	0.0	0	2.81	0.0
Chronic lymphocytic	0	0.26	0.0	0	0.51	0.0	0	0.35	0.0	0	0.37	0.0	0	1.51	0.0
Acute nonlymphocytic	0	0.11	0.0	0	0.24	0.0	0	0.16	0.0	0	0.18	0.0	0	0.70	0.0

[a] ICD-7 codes = 143–144.

[b] $P < .05$.

MOUTH
MALES

TABLE 4D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the gum or other mouth among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,035			730			301			141			1,035		
Person-yr in interval	894			1,728			1,071			1,022			4,715		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**13**	**10.94**	**1.2**	**34**	**21.75**	**1.6**[b]	**26**	**14.56**	**1.8**[b]	**17**	**15.24**	**1.1**	**90**	**62.49**	**1.4**[b]
All excluding site of initial cancer	**13**	**10.89**	**1.2**	**34**	**21.65**	**1.6**[b]	**26**	**14.50**	**1.8**[b]	**15**	**15.17**	**1.0**	**88**	**62.21**	**1.4**[b]
Buccal cavity, pharynx	**1**	**0.36**	**2.8**	**5**	**0.69**	**7.3**[b]	**1**	**0.44**	**2.3**	**5**	**0.43**	**11.5**[b]	**12**	**1.92**	**6.3**[b]
Lip	1	0.19	5.2	4	0.37	10.7[b]	1	0.24	4.2	1	0.23	4.3	7	1.04	6.8[b]
Tongue	0	0.03	0.0	1	0.05	19.2	0	0.03	0.0	1	0.03	31.7	2	0.14	13.9[b]
Salivary gland	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Gum, other mouth	0	0.05	0.0	0	0.10	0.0	0	0.06	0.0	2	0.07	30.0[b]	2	0.28	7.1
Pharynx	0	0.06	0.0	0	0.11	0.0	0	0.07	0.0	1	0.07	14.8	1	0.30	3.3
Digestive system	**6**	**4.29**	**1.4**	**12**	**8.41**	**1.4**	**8**	**5.59**	**1.4**	**6**	**5.59**	**1.1**	**32**	**23.88**	**1.3**
Esophagus	1	0.20	4.9	2	0.39	5.2	1	0.24	4.1	1	0.23	4.4	5	1.06	4.7[b]
Stomach	3	1.41	2.1	4	2.71	1.5	2	1.77	1.1	2	1.62	1.2	11	7.51	1.5
Colon	1	0.96	1.0	4	1.92	2.1	2	1.30	1.5	1	1.39	0.7	8	5.57	1.4
Rectum	1	0.95	1.0	1	1.87	0.5	2	1.23	1.6	2	1.23	1.6	6	5.27	1.1
Liver, biliary	0	0.22	0.0	0	0.44	0.0	0	0.31	0.0	0	0.34	0.0	0	1.31	0.0
Pancreas	0	0.41	0.0	1	0.83	1.2	1	0.57	1.7	0	0.62	0.0	2	2.43	0.8
Respiratory system	**3**	**2.08**	**1.4**	**12**	**4.19**	**2.9**[b]	**11**	**2.75**	**4.0**[b]	**1**	**3.05**	**0.3**	**27**	**12.07**	**2.2**[b]
Nasal cavities, sinuses	0	0.03	0.0	1	0.06	16.8	0	0.04	0.0	0	0.04	0.0	1	0.17	5.9
Larynx	0	0.15	0.0	1	0.29	3.5	0	0.18	0.0	0	0.20	0.0	1	0.82	1.2
Trachea, bronchus, lung	3	1.81	1.7	10	3.65	2.7[b]	9	2.40	3.8[b]	1	2.67	0.4	23	10.53	2.2[b]
Prostate gland	1	1.52	0.7	0	3.10	0.0	0	2.20	0.0	3	2.35	1.3	4	9.18	0.4
Testis	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.20	0.0
Kidney, renal pelvis, ureter	0	0.35	0.0	1	0.69	1.4	0	0.46	0.0	0	0.50	0.0	1	2.00	0.5
Bladder, other urinary	2	0.87	2.3	2	1.75	1.1	1	1.18	0.8	2	1.30	1.5	7	5.10	1.4
Melanoma of the skin	0	0.09	0.0	0	0.18	0.0	0	0.12	0.0	0	0.12	0.0	0	0.50	0.0
Eye	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.18	0.0
Brain, central nervous system	0	0.16	0.0	0	0.32	0.0	0	0.20	0.0	0	0.21	0.0	0	0.89	0.0
Thyroid gland	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.17	0.0
Bone	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.11	0.0
Connective tissue	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.21	0.0
Lymphatic, hematopoietic system	**0**	**0.69**	**0.0**	**1**	**1.38**	**0.7**	**2**	**0.93**	**2.1**	**0**	**1.00**	**0.0**	**3**	**4.00**	**0.8**
Non-Hodgkin's lymphoma	0	0.18	0.0	0	0.35	0.0	2	0.24	8.4	0	0.25	0.0	2	1.02	2.0
Hodgkin's disease	0	0.05	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.26	0.0
Multiple myeloma	0	0.13	0.0	1	0.26	3.9	0	0.18	0.0	0	0.19	0.0	1	0.75	1.3
Leukemias	0	0.33	0.0	0	0.66	0.0	0	0.45	0.0	0	0.48	0.0	0	1.93	0.0
Chronic lymphocytic	0	0.19	0.0	0	0.37	0.0	0	0.26	0.0	0	0.27	0.0	0	1.09	0.0
Acute nonlymphocytic	0	0.07	0.0	0	0.15	0.0	0	0.10	0.0	0	0.12	0.0	0	0.45	0.0

[a] ICD-7 codes = 143–144.

[b] $P < .05$.

MOUTH
FEMALES

TABLE 4E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the gum or other mouth among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	729			509			230			106			729		
Person-yr in interval	631			1,285			792			753			3,462		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**6.90**	**0.6**	**17**	**13.45**	**1.3**	**13**	**8.53**	**1.5**	**7**	**8.74**	**0.8**	**41**	**37.62**	**1.1**
All excluding site of initial cancer	**4**	**6.87**	**0.6**	**17**	**13.39**	**1.3**	**13**	**8.49**	**1.5**	**7**	**8.70**	**0.8**	**41**	**37.45**	**1.1**
Buccal cavity, pharynx	**0**	**0.10**	**0.0**	**0**	**0.19**	**0.0**	**2**	**0.12**	**16.9**[b]	**1**	**0.12**	**8.1**	**3**	**0.53**	**5.6**[b]
Lip	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Tongue	0	0.02	0.0	0	0.03	0.0	2	0.02	93.3[b]	1	0.02	43.3	3	0.10	30.5[b]
Salivary gland	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Gum, other mouth	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.17	0.0
Pharynx	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Digestive system	**1**	**2.70**	**0.4**	**8**	**5.12**	**1.6**	**6**	**3.28**	**1.8**	**0**	**3.35**	**0.0**	**15**	**14.45**	**1.0**
Esophagus	0	0.09	0.0	2	0.15	13.2[b]	1	0.10	10.5	0	0.10	0.0	3	0.44	6.9[b]
Stomach	0	0.75	0.0	1	1.35	0.7	0	0.86	0.0	0	0.81	0.0	1	3.78	0.3
Colon	1	0.82	1.2	4	1.59	2.5	2	1.03	2.0	0	1.10	0.0	7	4.53	1.5
Rectum	0	0.45	0.0	0	0.86	0.0	0	0.55	0.0	0	0.55	0.0	0	2.40	0.0
Liver, biliary	0	0.22	0.0	1	0.44	2.3	2	0.29	6.9	0	0.31	0.0	3	1.26	2.4
Pancreas	0	0.26	0.0	0	0.52	0.0	0	0.33	0.0	0	0.36	0.0	0	1.47	0.0
Respiratory system	**2**	**0.35**	**5.7**	**2**	**0.70**	**2.9**	**2**	**0.44**	**4.5**	**1**	**0.47**	**2.1**	**7**	**1.96**	**3.6**[b]
Nasal cavities, sinuses	1	0.01	92.7[b]	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	1	0.06	17.7
Larynx	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Trachea, bronchus, lung	1	0.29	3.4	2	0.59	3.4	2	0.37	5.4	1	0.40	2.5	6	1.65	3.6[b]
Female breast	0	1.34	0.0	1	2.64	0.4	0	1.66	0.0	2	1.72	1.2	3	7.35	0.4
Female genital tract	**1**	**1.07**	**0.9**	**3**	**2.18**	**1.4**	**1**	**1.34**	**0.7**	**1**	**1.33**	**0.8**	**6**	**5.93**	**1.0**
Cervix uteri	1	0.30	3.4	0	0.61	0.0	1	0.38	2.7	0	0.37	0.0	2	1.65	1.2
Corpus uteri	0	0.32	0.0	1	0.65	1.5	0	0.39	0.0	0	0.38	0.0	1	1.74	0.6
Uterus, NOS	0	0.04	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.18	0.0
Ovary, fallopian tubes	0	0.33	0.0	2	0.68	2.9	0	0.42	0.0	1	0.42	2.4	3	1.86	1.6
Kidney, renal pelvis, ureter	0	0.18	0.0	0	0.36	0.0	0	0.23	0.0	0	0.24	0.0	0	1.01	0.0
Bladder, other urinary	0	0.20	0.0	1	0.40	2.5	0	0.26	0.0	0	0.27	0.0	1	1.14	0.9
Melanoma of the skin	0	0.08	0.0	0	0.16	0.0	1	0.10	9.9	1	0.11	9.0	2	0.45	4.4
Eye	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Brain, central nervous system	0	0.11	0.0	1	0.22	4.6	0	0.14	0.0	1	0.14	7.4	2	0.60	3.3
Thyroid gland	0	0.05	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.27	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Connective tissue	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**0**	**0.36**	**0.0**	**1**	**0.73**	**1.4**	**0**	**0.47**	**0.0**	**0**	**0.50**	**0.0**	**1**	**2.07**	**0.5**
Non-Hodgkin's lymphoma	0	0.11	0.0	0	0.22	0.0	0	0.14	0.0	0	0.15	0.0	0	0.62	0.0
Hodgkin's disease	0	0.02	0.0	1	0.05	21.8	0	0.03	0.0	0	0.03	0.0	1	0.13	7.9
Multiple myeloma	0	0.07	0.0	0	0.15	0.0	0	0.10	0.0	0	0.10	0.0	0	0.42	0.0
Leukemias	0	0.16	0.0	0	0.31	0.0	0	0.20	0.0	0	0.21	0.0	0	0.88	0.0
Chronic lymphocytic	0	0.07	0.0	0	0.14	0.0	0	0.09	0.0	0	0.10	0.0	0	0.42	0.0
Acute nonlymphocytic	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.25	0.0

[a] ICD-7 codes = 143–144.

[b] $P < .05$.

PHARYNX
BOTH SEXES

TABLE 5A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the pharynx, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,289	568	1,857
No. who developed a second primary cancer	51	17	68
Average age at diagnosis of first cancer, yr	61	61	61
Average yr of diagnosis of first cancer	1965	1964	1965
Person-yr of follow-up	3,743	2,168	5,911
Average follow-up, yr	2.9	3.8	3.2
Percent given radiotherapy for first cancer	91	89	90

[a] ICD-7 codes = 145–148.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 5B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the pharynx in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	57	83.8
Only the first cancer	9	13.2
Only the second cancer	2	2.9
Neither first nor second cancer	0	0.0
Total second primary cancers	68	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

PHARYNX
BOTH SEXES

TABLE 5C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pharynx among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,857			1,113			318			143			1,857		
Person-yr in interval	1,491			2,214			1,093			1,113			5,910		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**9**	**13.70**	**0.7**	**33**	**19.81**	**1.7**[b]	**15**	**10.38**	**1.4**	**11**	**11.44**	**1.0**	**68**	**55.32**	**1.2**
All excluding site of initial cancer	**9**	**13.63**	**0.7**	**33**	**19.72**	**1.7**[b]	**15**	**10.34**	**1.5**	**11**	**11.40**	**1.0**	**68**	**55.07**	**1.2**
Buccal cavity, pharynx	**0**	**0.40**	**0.0**	**1**	**0.54**	**1.9**	**1**	**0.25**	**4.0**	**1**	**0.27**	**3.7**	**3**	**1.47**	**2.0**
Lip	0	0.20	0.0	0	0.25	0.0	1	0.12	8.3	0	0.12	0.0	1	0.69	1.4
Tongue	0	0.04	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.14	0.0
Salivary gland	0	0.04	0.0	1	0.06	16.7	0	0.03	0.0	0	0.03	0.0	1	0.15	6.7
Gum, other mouth	0	0.06	0.0	0	0.08	0.0	0	0.05	0.0	1	0.05	20.0	1	0.24	4.2
Pharynx	0	0.07	0.0	0	0.09	0.0	0	0.04	0.0	0	0.04	0.0	0	0.25	0.0
Digestive system	**1**	**5.12**	**0.2**	**10**	**7.07**	**1.4**	**4**	**3.69**	**1.1**	**5**	**4.00**	**1.3**	**20**	**19.89**	**1.0**
Esophagus	0	0.23	0.0	1	0.28	3.6	1	0.14	7.1	0	0.15	0.0	2	0.80	2.5
Stomach	0	1.62	0.0	1	2.08	0.5	1	1.04	1.0	1	1.01	1.0	3	5.73	0.5
Colon	1	1.21	0.8	2	1.78	1.1	0	0.97	0.0	2	1.14	1.8	5	5.11	1.0
Rectum	0	1.09	0.0	3	1.49	2.0	0	0.76	0.0	1	0.81	1.2	4	4.15	1.0
Liver, biliary	0	0.30	0.0	2	0.46	4.3	1	0.26	3.8	0	0.32	0.0	3	1.32	2.3
Pancreas	0	0.50	0.0	1	0.73	1.4	1	0.39	2.6	0	0.46	0.0	2	2.08	1.0
Respiratory system	**4**	**2.23**	**1.8**	**7**	**3.22**	**2.2**	**5**	**1.60**	**3.1**[b]	**2**	**1.79**	**1.1**	**18**	**8.83**	**2.0**[b]
Nasal cavities, sinuses	0	0.04	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Larynx	0	0.16	0.0	2	0.22	9.1[b]	1	0.11	9.1	0	0.11	0.0	3	0.59	5.1[b]
Trachea, bronchus, lung	4	1.93	2.1	5	2.81	1.8	4	1.40	2.9	2	1.57	1.3	15	7.70	1.9[b]
Female breast	0	0.76	0.0	2	1.37	1.5	0	0.82	0.0	1	0.94	1.1	3	3.88	0.8
Female genital tract	**0**	**0.70**	**0.0**	**2**	**1.27**	**1.6**	**0**	**0.73**	**0.0**	**0**	**0.80**	**0.0**	**2**	**3.49**	**0.6**
Cervix uteri	0	0.23	0.0	2	0.41	4.9	0	0.22	0.0	0	0.23	0.0	2	1.09	1.8
Corpus uteri	0	0.20	0.0	0	0.37	0.0	0	0.22	0.0	0	0.24	0.0	0	1.03	0.0
Uterus, NOS	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Ovary, fallopian tubes	0	0.20	0.0	0	0.38	0.0	0	0.22	0.0	0	0.25	0.0	0	1.06	0.0
Prostate gland	0	1.26	0.0	3	1.64	1.8	2	0.82	2.4	0	0.90	0.0	5	4.63	1.1
Testis	0	0.05	0.0	1	0.07	14.3	0	0.03	0.0	0	0.04	0.0	1	0.19	5.3
Kidney, renal pelvis, ureter	1	0.42	2.4	2	0.61	3.3	0	0.32	0.0	0	0.36	0.0	3	1.72	1.7
Bladder, other urinary	1	0.90	1.1	0	1.29	0.0	2	0.66	3.0	0	0.75	0.0	3	3.59	0.8
Melanoma of the skin	0	0.14	0.0	0	0.22	0.0	0	0.11	0.0	0	0.13	0.0	0	0.60	0.0
Eye	0	0.04	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.16	0.0
Brain, central nervous system	0	0.25	0.0	2	0.39	5.1	1	0.20	5.0	0	0.21	0.0	3	1.04	2.9
Thyroid gland	1	0.05	20.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	1	0.24	4.2
Bone	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Connective tissue	0	0.05	0.0	0	0.07	0.0	0	0.03	0.0	0	0.03	0.0	0	0.19	0.0
Lymphatic, hematopoietic system	**1**	**0.83**	**1.2**	**3**	**1.20**	**2.5**	**0**	**0.64**	**0.0**	**2**	**0.73**	**2.7**	**6**	**3.40**	**1.8**
Non-Hodgkin's lymphoma	1	0.22	4.5	2	0.33	6.1	0	0.18	0.0	0	0.20	0.0	3	0.93	3.2
Hodgkin's disease	0	0.06	0.0	0	0.09	0.0	0	0.05	0.0	0	0.05	0.0	0	0.26	0.0
Multiple myeloma	0	0.16	0.0	0	0.23	0.0	0	0.12	0.0	0	0.14	0.0	0	0.63	0.0
Leukemias	0	0.38	0.0	1	0.54	1.9	0	0.28	0.0	2	0.33	6.1	3	1.53	2.0
Chronic lymphocytic	0	0.20	0.0	0	0.27	0.0	0	0.14	0.0	1	0.16	6.3	1	0.79	1.3
Acute nonlymphocytic	0	0.09	0.0	1	0.14	7.1	0	0.08	0.0	0	0.10	0.0	1	0.41	2.4

[a] ICD-7 codes = 145–148.

[b] $P < .05$.

PHARYNX
MALES

TABLE 5D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pharynx among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,289			781			187			82			1,289		
Person-yr in interval	1,043			1,420			640			640			3,743		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	9	10.06	0.9	21	13.26	1.6	12	6.34	1.9	9	6.75	1.3	51	36.40	1.4[b]
All excluding site of initial cancer	9	10.00	0.9	21	13.19	1.6	12	6.31	1.9	9	6.72	1.3	51	36.20	1.4[b]
Buccal cavity, pharynx	0	0.35	0.0	0	0.45	0.0	1	0.20	4.9	1	0.21	4.8	2	1.21	1.7
Lip	0	0.19	0.0	0	0.24	0.0	1	0.11	9.1	0	0.11	0.0	1	0.65	1.5
Tongue	0	0.03	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.09	0.0
Salivary gland	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Gum, other mouth	0	0.05	0.0	0	0.06	0.0	0	0.03	0.0	1	0.03	32.2	1	0.17	5.9
Pharynx	0	0.06	0.0	0	0.07	0.0	0	0.03	0.0	0	0.03	0.0	0	0.20	0.0
Digestive system	1	3.85	0.3	7	4.83	1.4	2	2.26	0.9	4	2.32	1.7	14	13.26	1.1
Esophagus	0	0.19	0.0	1	0.22	4.5	1	0.10	10.0	0	0.10	0.0	2	0.61	3.3
Stomach	0	1.26	0.0	1	1.48	0.7	0	0.67	0.0	1	0.65	1.5	2	4.05	0.5
Colon	1	0.84	1.2	1	1.10	0.9	0	0.53	0.0	1	0.57	1.8	3	3.04	1.0
Rectum	0	0.87	0.0	3	1.09	2.7	0	0.51	0.0	1	0.52	1.9	4	2.99	1.3
Liver, biliary	0	0.20	0.0	1	0.27	3.7	0	0.13	0.0	0	0.15	0.0	1	0.74	1.3
Pancreas	0	0.38	0.0	0	0.51	0.0	1	0.25	4.0	0	0.27	0.0	1	1.40	0.7
Respiratory system	4	2.05	2.0	7	2.88	2.4	4	1.39	2.9	2	1.53	1.3	17	7.84	2.2[b]
Nasal cavities, sinuses	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Larynx	0	0.15	0.0	2	0.21	9.7[b]	1	0.10	10.4	0	0.10	0.0	3	0.55	5.4[b]
Trachea, bronchus, lung	4	1.78	2.2	5	2.52	2.0	3	1.22	2.5	2	1.35	1.5	14	6.86	2.0[b]
Prostate gland	0	1.26	0.0	3	1.64	1.8	2	0.82	2.4	0	0.90	0.0	5	4.63	1.1
Testis	0	0.05	0.0	1	0.07	14.3	0	0.03	0.0	0	0.04	0.0	1	0.19	5.3
Kidney, renal pelvis, ureter	1	0.33	3.1	2	0.44	4.5	0	0.21	0.0	0	0.23	0.0	3	1.22	2.5
Bladder, other urinary	1	0.80	1.3	0	1.11	0.0	2	0.54	3.7	0	0.60	0.0	3	3.05	1.0
Melanoma of the skin	0	0.09	0.0	0	0.13	0.0	0	0.06	0.0	0	0.07	0.0	0	0.35	0.0
Eye	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Brain, central nervous system	0	0.18	0.0	0	0.26	0.0	1	0.12	8.5	0	0.13	0.0	1	0.68	1.5
Thyroid gland	1	0.03	34.9	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	1	0.11	9.4
Bone	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Connective tissue	0	0.04	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Lymphatic, hematopoietic system	1	0.65	1.6	1	0.86	1.2	0	0.42	0.0	2	0.45	4.5	4	2.38	1.7
Non-Hodgkin's lymphoma	1	0.17	5.9	1	0.23	4.3	0	0.11	0.0	0	0.12	0.0	2	0.63	3.2
Hodgkin's disease	0	0.05	0.0	0	0.07	0.0	0	0.03	0.0	0	0.03	0.0	0	0.19	0.0
Multiple myeloma	0	0.12	0.0	0	0.16	0.0	0	0.08	0.0	0	0.08	0.0	0	0.43	0.0
Leukemias	0	0.30	0.0	0	0.40	0.0	0	0.19	0.0	2	0.21	9.7[b]	2	1.10	1.8
Chronic lymphocytic	0	0.17	0.0	0	0.21	0.0	0	0.10	0.0	1	0.11	9.0	1	0.60	1.7
Acute nonlymphocytic	0	0.07	0.0	0	0.10	0.0	0	0.05	0.0	0	0.06	0.0	0	0.28	0.0

[a] ICD-7 codes = 145–148.
[b] $P < .05$.

PHARYNX
FEMALES

TABLE 5E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pharynx among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	568			332			131			61			568		
Person-yr in interval	448			794			452			473			2,168		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**0**	**3.64**	**0.0**	**12**	**6.55**	**1.8**	**3**	**4.04**	**0.7**	**2**	**4.69**	**0.4**	**17**	**18.92**	**0.9**
All excluding site of initial cancer	**0**	**3.63**	**0.0**	**12**	**6.53**	**1.8**	**3**	**4.03**	**0.7**	**2**	**4.68**	**0.4**	**17**	**18.87**	**0.9**
Buccal cavity, pharynx	**0**	**0.05**	**0.0**	**1**	**0.09**	**11.2**	**0**	**0.05**	**0.0**	**0**	**0.06**	**0.0**	**1**	**0.26**	**3.9**
Lip	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Tongue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Salivary gland	0	0.01	0.0	1	0.02	51.4	0	0.01	0.0	0	0.01	0.0	1	0.05	18.5
Gum, other mouth	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Pharynx	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Digestive system	**0**	**1.27**	**0.0**	**3**	**2.24**	**1.3**	**2**	**1.43**	**1.4**	**1**	**1.68**	**0.6**	**6**	**6.63**	**0.9**
Esophagus	0	0.04	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.19	0.0
Stomach	0	0.36	0.0	0	0.60	0.0	1	0.37	2.7	0	0.36	0.0	1	1.68	0.6
Colon	0	0.37	0.0	1	0.68	1.5	0	0.44	0.0	1	0.57	1.8	2	2.07	1.0
Rectum	0	0.22	0.0	0	0.40	0.0	0	0.25	0.0	0	0.29	0.0	0	1.16	0.0
Liver, biliary	0	0.10	0.0	1	0.19	5.4	1	0.13	7.8	0	0.17	0.0	2	0.58	3.4
Pancreas	0	0.12	0.0	1	0.22	4.6	0	0.14	0.0	0	0.19	0.0	1	0.68	1.5
Respiratory system	**0**	**0.18**	**0.0**	**0**	**0.34**	**0.0**	**1**	**0.21**	**4.7**	**0**	**0.26**	**0.0**	**1**	**0.99**	**1.0**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Larynx	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Trachea, bronchus, lung	0	0.15	0.0	0	0.29	0.0	1	0.18	5.6	0	0.22	0.0	1	0.84	1.2
Female breast	0	0.76	0.0	2	1.37	1.5	0	0.82	0.0	1	0.94	1.1	3	3.88	0.8
Female genital tract	**0**	**0.70**	**0.0**	**2**	**1.27**	**1.6**	**0**	**0.73**	**0.0**	**0**	**0.80**	**0.0**	**2**	**3.49**	**0.6**
Cervix uteri	0	0.23	0.0	2	0.41	4.9	0	0.22	0.0	0	0.23	0.0	2	1.09	1.8
Corpus uteri	0	0.20	0.0	0	0.37	0.0	0	0.22	0.0	0	0.24	0.0	0	1.03	0.0
Uterus, NOS	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Ovary, fallopian tubes	0	0.20	0.0	0	0.38	0.0	0	0.22	0.0	0	0.25	0.0	0	1.06	0.0
Kidney, renal pelvis, ureter	0	0.09	0.0	0	0.17	0.0	0	0.11	0.0	0	0.13	0.0	0	0.50	0.0
Bladder, other urinary	0	0.10	0.0	0	0.18	0.0	0	0.12	0.0	0	0.15	0.0	0	0.54	0.0
Melanoma of the skin	0	0.05	0.0	0	0.09	0.0	0	0.05	0.0	0	0.06	0.0	0	0.25	0.0
Eye	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Brain, central nervous system	0	0.07	0.0	2	0.13	15.5[b]	0	0.08	0.0	0	0.08	0.0	2	0.36	5.6
Thyroid gland	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Connective tissue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Lymphatic, hematopoietic system	**0**	**0.18**	**0.0**	**2**	**0.34**	**5.9**	**0**	**0.22**	**0.0**	**0**	**0.28**	**0.0**	**2**	**1.02**	**2.0**
Non-Hodgkin's lymphoma	0	0.05	0.0	1	0.10	9.8	0	0.07	0.0	0	0.08	0.0	1	0.30	3.3
Hodgkin's disease	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Multiple myeloma	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.06	0.0	0	0.20	0.0
Leukemias	0	0.08	0.0	1	0.14	7.1	0	0.09	0.0	0	0.12	0.0	1	0.43	2.3
Chronic lymphocytic	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.19	0.0
Acute nonlymphocytic	0	0.02	0.0	1	0.04	24.4	0	0.03	0.0	0	0.04	0.0	1	0.13	8.0

[a] ICD-7 codes = 145–148.

[b] $P < .05$.

Second Cancer Following Cancer of the Digestive System in Denmark, 1943–80 [1]

Elsebeth Lynge, Ole M. Jensen, *and* Bendix Carstensen [2]

ABSTRACT—Among 4,184 patients with cancer of the esophagus, 55 second primary cancers were observed, whereas 64 were expected [relative risk (RR) = 0.86]. The absence of an excess risk of alcohol- and tobacco-related cancers was not anticipated. A significant 19% deficit of second cancers was found among 30,843 patients with stomach cancer. Cancers of the rectum, kidney, and lung all occurred significantly below expectation. An excess risk of ovarian cancer (RR = 1.9) was seen in women. Reasons for these findings are not entirely clear. Cancer of the small intestine is rare, and despite a relatively short survival expectation, a moderate excess of second cancers was seen among 868 patients (36 vs. 26.8). Only cancers of the liver and gallbladder were significantly elevated, and the possibility of misclassified metastases is discussed. Colon cancer is one of the most common cancers in Denmark, and 29,490 patients with this disease were at slightly lower risk for development of second cancer (RR = 0.96; 95% confidence interval = 0.9–1.0) than the general Danish population, excluding secondary colon cancers. Esophageal, stomach, and liver cancers occurred less frequently than expected. That cancers of the uterine corpus and ovary were significantly increased supports the notion that common risk factors, such as diet and endogenous hormones, influence the development of these cancers. A significant 23% deficit of second cancers was also found among 26,597 patients with cancer of the rectum, excluding secondary rectal cancer. Significant deficits were seen for cancers of the stomach (RR = 0.5), lung (RR = 0.8), and brain (RR = 0.5), and for multiple myeloma (RR = 0.4). The likelihood of underreporting of second cancers, especially of the digestive system, is discussed. However, cancer of sites previously reported to be associated with rectal cancer, e.g., the colon, breast, and uterus, did not occur below expectation. Cancers of the liver and biliary tract occurred in 4,453 patients; their average survival was only 1 year. Except for a slight excess of cancer of the ovary (5 vs. 1.6), the risk of second cancer development for all sites was consistent with unity (RR = 0.90). The risk of second cancers among 7,752 persons with cancer of the pancreas was not greater than expected (88 vs. 85.2). Males were at significant risk of kidney cancer (RR = 3.2), whereas females showed elevated rates of cancers of the uterine corpus (RR = 3.2) and ovary (RR = 3.1). No site occurred significantly below expectation.—Natl Cancer Inst Monogr 68: 277–308, 1985.

ESOPHAGUS (ICD-7, 150)

Cancer of the esophagus accounts for only 0.6% of all cancers in men and 0.3% in women. The age-standardized incidence rates/100,000 are 2.9 for men and 1.1 for women and yield a male-to-female ratio of 2.6 (*1*). Incidence rates for men are two times higher in Copenhagen than in rural areas, whereas no substantial urban–rural difference has been seen among women. Since 1943, the incidence of esophageal cancer has decreased among women until the present and until the end of the 1960s among men (*2*). In the mid-1940s, 40% of esophageal cancer cases were histologically verified in contrast to 91% today (*1, 3*). The fatality rate for this neoplasm is high, with the 5-year relative survival rate ranging from 7 to 8% in men and women. Little improvement in survival has occurred over the past decades (*4*).

The predominant risk factors for esophageal cancer are alcohol and tobacco (*5*). The risk is especially high among persons with heavy exposure to both, and it is estimated that approximately 70% of all these cancers can be attributed to these 2 factors. The consumption of hard liquor has been strongly associated with a high risk of esophageal cancer, but indications have been reported (*6*) that weaker alcoholic beverages such as beer also lead to increases in risk. Beer is the preferred alcoholic beverage in Denmark, with the consumption of wine and strong spirits increasing during past decades (*7*). The Plummer-Vinson syndrome, low fruit and vegetable consumption, poor nutrition in general, and ionizing radiation have also been suggested as risk factors for esophageal cancer (*8*).

Results

During 1943–80, of the 4,184 persons reported to the Registry with cancer of the esophagus and included in the present study, approximately two-thirds were men. The average age at diagnosis was 68 years for males and 71 years for females. The average follow-up period was 1.2 years with little difference between the 2 sexes. Radiotherapy was received by 50% of the patients as initial treatment, and 30% of them were treated by some surgical procedure which could be either palliative or curative. Among men, 33 second cancers were recorded, whereas 40.9 were expected (RR = 0.8; 95% CI = 0.6–1.1). Among women, 22 second cancers were observed in contrast to 23.1 expected (RR = 1.0; 95% CI = 0.6–1.4). Cancers of the digestive system as a whole, disregarding the index cancer, occurred significantly less often than expected (n = 13, E = 24.8). Only kidney cancer in men (RR = 3.9; 95% CI = 1.3–9.1) was significantly elevated. No excess of this tumor was seen among women, but a slight increase in their risk of breast cancer was seen (RR = 1.6; 95% CI = 0.6–3.3).

Discussion

Persons with esophageal cancer showed a slight deficit of subsequent second cancers. No site was increased above

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ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; RR = relative risk(s); E = expected number of cancers; CI = confidence interval.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Elsebeth Lynge.

expectation except for kidney among men. This association has not been described previously, and the absence of a similar observation for women suggests a chance occurrence related to the high number of comparisons. Among women, the risk of breast cancer increased with time since diagnosis of esophageal cancer, but only 39 patients survived more than 10 years and the trend was not significant. Because 50% of the women received radiotherapy as the initial treatment, the slight increase in breast cancer risk could be associated with this exposure. This would be in line with the observation of an increased breast cancer risk among women who have received various radiation exposures (*9*).

In view of the well-established relationship between esophageal cancer and alcohol and tobacco consumption (*1*), the most striking finding in our study is the absence of an increased risk of other cancers known to be associated with these 2 factors either alone or in combination. Only a slight, insignificant increased risk of cancer of the buccal cavity, pharynx, and larynx was indicated, and the risk of primary lung cancer was not increased. However, numbers are small and the average survival time is only about 1 year. In addition, clinicians and personnel in the Registry may have been reluctant to accept cancers of these organs as truly new tumors (*10*). They may have interpreted such tumors as extensions or metastases from the first cancer, thus underestimating the risks. Our findings are different from previous studies, which have indicated an increased risk of cancers of the upper respiratory and digestive tract in patients with esophageal cancer (*11*).

STOMACH (ICD-7, 151)

The incidence of stomach cancer in Denmark has been declining since World War II (*12*). The reduced intake of salted meat and fish and the increased intake of vegetables, fruits, and ascorbic acid have been suggested as reasons for this decline, although the etiology of this disease is still largely unknown (*12*). Despite the reduction in incidence, stomach cancer remains important in Denmark, where it accounts for 4% of all cancers (*1*). The age-standardized incidence is 15.1 and 7.0/100,000 for men and women, respectively, which gives a male-to-female ratio of 2.2. In the 1940s, only 18% of the stomach cancers were histologically verified in contrast to 85% today (*1, 3*); some of the decline in incidence may have been due to improved diagnostic techniques (*13*).

Results

A total of 30,843 stomach cancers, reported to the Registry between 1943 and 1980, are included in the study. The average age at diagnosis was 67 years for men and 70 years for women. On average, the patients had been observed for 1.9 years. Only 4% of the stomach cancer patients received radiotherapy, whereas 57% were treated surgically. Among patients with stomach cancer, 521 second cancers were recorded as opposed to an expected number of 643.1 when the observed and expected number of second stomach cancers were excluded from the tabulations (RR = 0.81; 95% CI = 0.74–0.88). Cancers of the rectum (RR = 0.7), kidney (RR = 0.6), and lung (RR = 0.7) all occurred significantly below expectation. In women, we saw an increased risk of ovarian cancer (RR = 1.9; 95% CI = 1.2–2.9), and an excess of pancreatic cancer ($n = 39$, $E = 28.3$) was suggested in both men and women (RR = 1.4; 95% CI = 0.9–2.1).

Discussion

An overall deficit of second cancer, observed among patients with stomach cancer, could not be attributed to any specific site, although decreased risks were especially noticeable for cancers of the rectum, kidney, and lung. A borderline significant excess risk of pancreatic cancer was seen in both men and women, and most cancers were diagnosed more than 5 years after the stomach cancer. It seems unlikely that the excess should be due to pancreatic cancers that were misdiagnosed as stomach cancers, but the association is at the moment unexplained. The excess number of ovarian cancers might partly stem from misdiagnosed or misregistered metastases from the stomach cancer, the so-called Krukenberg tumors.

SMALL INTESTINE (ICD-7, 152)

Incidence rates of the rarely seen cancer of the small intestine in 1978–80 were 0.9 and 0.7 cases/100,000 among males and females, respectively (*1*). The incidence of this disease has increased slightly over time. In 1943, 38% of the cancers of the small intestine were histologically verified versus 96% in 1980 (*1, 3*). Lymphomas of the small intestine are included with the category of non-Hodgkin's lymphoma and not with cancer of the small intestine. Little is known about the etiology of cancer of the small intestine, but the pattern of occurrence indicates risk factors similar to those of colon cancer (*14*). Adenocarcinomas have been associated also with Crohn's disease, but the etiology of carcinoids is virtually unknown.

Results

A total of 868 patients with cancer of the small intestine were included in the present study. They were diagnosed on average at the age of 63 years; the average follow-up was 2.9 years. Radiation treatment was received by 6% of all patients and 71% had surgical treatment. If one considers the relatively short follow-up, the moderate 34% excess risk of second cancers observed is interesting. A total of 36 second primary tumors occurred compared with 26.8 expected cases (RR = 1.34; 95% CI = 0.94–1.86). The cancer patterns were similar for males and females. Sixteen (or 44%) of the observed second cancers were located in the digestive organs with nonsignificant excess risks observed for colon, rectum, and pancreatic cancer, and a significant excess risk for cancer of the liver and biliary tract (RR = 5.7; 95% CI = 1.6–15). A borderline significant increased risk for cancer of the ovary was also observed (RR = 4.8; 95% CI = 1.0–14).

Discussion

Patients with cancer of other parts of the digestive tract were apparently at decreased risk of developing a second primary cancer, whereas patients with cancer of the small intestine were at an increased risk for a subsequent tumor. The observed 34% excess, however, was not statistically significant. About one-half of the cancers of the small intestine seen in patients in Denmark are adenocarcinomas, and the excess of liver and biliary tract cancer should be evaluated in light of the fact that the most frequent metastatic sites for these adenocarcinomas are the regional lymph nodes and the liver (*14*). A portion of the excess of ovarian cancer might also be due to misdiagnosed metastases. Because the rates of cancer of the small intestine vary closely with those of colon cancer and suggest a common etiology, the fact that colon cancer is one of the sites showing a slight excess risk in the present study should arouse interest. This is in line with results of a previous study from the Connecticut Tumor Registry (*11*). Excesses seen for cancers of the liver and ovary in our survey were also found in Connecticut.

COLON INCLUDING RECTOSIGMOID (ICD-7, 153)

As one of the most common cancers in Denmark with an annual incidence rate of 20.5 cases/100,000 persons for men and women (*1*), colon cancer has increased slightly since the mid-1940s, during which time 34% of the cases were histologically verified in contrast to 89% today (*1, 3*). During the same period, the incidence of rectal cancer decreased slightly. Approximately 40% of the colon cancers registered in Denmark are located in the sigmoid colon including the rectosigmoid junction. A possible change in the clinical classification of colon and rectum tumors over time might have contributed to the increasing and decreasing trends of colon and rectal cancer, respectively.

The international variation in colon cancer patterns, supplemented with observations of high- and low-risk groups, suggests that diets of affluent Western societies are associated with risk of this neoplasm (*15*). Internationally, consumption of meat and animal fat is positively correlated with the occurrence of colon cancer, whereas the opposite is true for consumption of cereals (*16*). An etiologic role of fat in the causation of colon cancer is further suggested in case-control studies and in population comparisons, including examinations of fecal bile acids possibly excreted and converted in the gut to co-carcinogens in response to fat intake (*17*). Conditions associated with a high risk of colon cancer include ulcerative colitis and familial polyposis. Colon cancer has been included in a cancer family syndrome which also encompasses cancers of the ovary and endometrium (*18*).

Results

A total of 29,490 colon cancer patients were included in this study and followed for 3.8 years on average. Only 4% had radiation therapy, whereas 82% were treated by curative or palliative surgery. From the beginning of the Registry, the location of the tumor in the colon has been specified in the code. However, it is uncertain how second primary cancers within the colon were registered before 1978, particularly if the location differed from that of the initial tumor. After 1978, both simultaneous and nonsimultaneous tumors of other segments of the colon have been regarded as independent primary cancers. In our study, 110 second colon cancers were reported compared with 146.1 expected cases, i.e., a 25% deficit of new colon cancers. As the different parts of the colon were not specified in this publication, and as there were uncertainties with regard to the recording of nonsimultaneous colon cancers, both the observed and the expected second colon cancers have been excluded in the evaluation of the overall risk.

A total of 1,179 second cancers of other organs were observed versus 1,224 expected (RR = 0.96; 95% CI = 0.91–1.02). Men showed a slight deficit of new cancers (RR = 0.9), whereas the occurrence of second cancers among women was equal to that expected (RR = 1.0). The observed number of cancers of digestive organs other than colon was lower than expected (RR = 0.9; 95% CI = 0.8–1.0) as a result of decreased RR for cancers of the esophagus (0.6), stomach (0.7), and liver and biliary tract (0.8). Only the risk of stomach cancer was significantly lower than predicted on the basis of rates prevailing in the general population. The risk for rectal cancer was slightly increased (RR = 1.2; 95% CI = 0.95–1.4).

Among male patients with colon cancer, no excess of second cancers was observed for any site. However, statistically significant increased risks were found among females for cancers of the corpus uteri (RR = 1.8; 95% CI = 1.3–2.3) and ovary (RR = 2.6; 95% CI = 2.1–3.1). For cancer of the corpus uteri, the excess was seen mainly between 1 and 10 years after the colon cancer developed, and, for cancer of the ovary, the excess was seen mainly within the first 5 years after the colon cancer was diagnosed.

Discussion

In evaluating the deficit of second cancers diagnosed in the digestive system among colon cancer patients, one should consider the low proportion of histologically verified cases during the early years of the registration period. A high proportion, i.e., 94%, of the colon cancer patients registered with a second cancer had a histologically verified colon cancer. This higher proportion of histologic confirmation in patients with multiple tumors may reflect a certain reluctance among reporting physicians and Registry personnel to accept second cancers in the digestive tract among patients with colon cancers whose tumors have not been microscopically verified.

An increased risk for cancers of the breast, corpus uteri, and ovary among women with colorectal cancer has been recorded previously (*19*). Except for a slight deficit of breast cancer (RR = 0.9; 95% CI = 0.8–1.1), the present data are consistent with these findings. Reduced fertility and intake of a high fat diet have been suggested as common etiology for these 4 cancers that are possibly mediated by endocrine factors (*20, 21*). Cancer-prone families often have a similar constellation of tumors including stomach cancer, which was, however, significantly decreased in the present investigation. This latter finding is in line with the inverse international correlation between colon and stomach cancers (*17*).

RECTUM EXCLUDING RECTOSIGMOID (ICD-7, 154)

Cancer of the rectum is another of the common cancers in Denmark. The incidence (*1*) is higher among males (16.1/100,000) than among females (10.0/100,000). The Danish rates are among the highest in the world (*22*). The incidence of rectal cancer has decreased slightly over time, but this has to be evaluated in light of the increasing trend for colon cancer. During the 1940s, 60% of rectal cancer cases were histologically verified compared with 93% today (*1, 3*). Internationally, the occurrence of rectal cancer is highly correlated with colon cancer (*17*). Rectal cancer also shows the same variation with food consumption as colon cancer, and it has been suggested that cancers of the colon and rectum may share a number of risk factors (*19*). These include medical conditions such as familial polyposis and inflammatory bowel disease. On the basis of the consistently higher male-to-female ratios for rectal than for colon cancer, however, it also has been suggested that the etiology differs slightly (*15*). Beer drinking has been thought to increase the risk of rectal cancer (*23*), but this could not be confirmed in a Danish study (*24*).

Results

The 15,442 men with rectal cancer included in the present study were followed on average for 3.8 years. The 11,155 women were followed for an average of 4.4 years. The average age at diagnosis was 67 years. For both sexes, 11% of the patients had radiation treatment and 81% were treated surgically.

A total of 968 second cancers developed in patients with rectal cancer compared with 1,258 expected cases. Both as a result of surgical removal of the rectum in a large proportion of patients and the recording practices of the Registry, it was unlikely that a second rectal cancer would be registered. This statement is reflected in the fact that no second rectal cancer was registered during 37 years of Registry operation covered in this analysis. The expected second rectal cancers have therefore been excluded from the analysis.

Excluding the rectum, 278 cancers of the digestive system were observed versus 412 expected. Deficits were seen for cancers of the esophagus, stomach, liver, and pancreas but not for the colon (RR = 1.0; 95% CI = 0.8-1.2). Significant deficits were also found for cancers of the lung (RR = 0.8), and brain (RR = 0.5), and for multiple myeloma (RR = 0.4). No single cancer site was found to be significantly in excess. Among women, cancers of the breast (RR = 1.0), corpus uteri (RR = 1.1), and ovary (RR = 1.1) were at a level similar to that found in the female population in general.

Discussion

The 23% deficit of all second cancers among patients with rectal cancer is remarkable and may be partly related to reporting and coding practices of second cancers, particularly of the digestive system, in Denmark. Those cancers which do not show deficits are those previously reported to be associated with the occurrence of rectum cancer, i.e., cancers of the colon, breast, corpus uteri, and ovary (*19*). The reasons for the significant deficit of lung cancer are not clear. The significant deficits of brain cancer and multiple myeloma were unexpected and might be chance findings associated with the large number of comparisons made.

LIVER AND BILIARY TRACT (ICD-7, 155)

Primary tumors of hepatocellular origin or arising in the biliary tract, including the gallbladder and ampulla of Vater, are rare in Denmark and account for only 1.9 and 2.6% of all cancers in men and women, respectively. Although the age-standardized incidence rates for liver cancer are 1.5 times higher in men than in women, 3.4 and 2.2/100,000, respectively, the reverse is true for biliary tract cancer with rates of 1.9 and 3.0/100,000 for men and women (*1*). Trends and regional differences in the occurrence of these tumors are difficult for one to evaluate because they depend heavily on diagnostic facilities and the frequency of autopsies. The proportion of histologically verified liver cancers has increased over time from a relatively low proportion in the 1940s to 89% today; confirmation of cancers of the biliary tract has increased from 56 to 89% (*1, 3*).

Risk factors for primary liver cancer and biliary tract cancer are generally not well known. Cirrhosis of the liver is regarded as a precursor lesion for hepatoma development, and alcohol may thus be associated indirectly with this tumor, as may other cirrhogenic exposures (*5*). Hepatitis B infection has also attracted much attention as a possible liver carcinogen (*25*). Although the proportion of hepatomas that may be attributable to these risk factors is unknown, it is generally believed that exposure to the well-known liver carcinogen aflatoxin is of minor importance in Denmark. Biliary tract tumors have been associated with the consumption of dietary fat, obesity, and the prevalence of gallstones (*26*).

Results

A total of 4,453 persons were reported to the Registry with cancers of the liver (678 men, 549 women) and biliary tract (963 men, 2,262 women) between 1943 and 1980 and are included in the present study. The average year of diagnosis for the 2 cancer sites was 1966, and the average age at diagnosis was 67 years. The average follow-up was 1 year after the time of diagnosis, and 4,297 person-years of observation were available for analysis. Only 74 persons were followed for 10 or more years. Only 4% of the persons with cancer of the liver and the biliary tract received radiotherapy. A considerable difference existed between the 2 cancer sites in the proportion of patients treated surgically: 60% of the persons with biliary tract tumors versus 20% of those with liver cancer. Eighty percent of both first and second cancers were histologically verified among patients who developed multiple tumors. All 5 patients with second primary cancer following hepatoma had both the first and the second primary histologically verified.

Overall 45 second cancers were recorded in patients with cancer of the liver and gallbladder in contrast to 49.9

expected (RR = 0.90; 95% CI = 0.66–1.21). The observed number of new cancers did not significantly exceed the expected number for any site, except for cancer of the ovary (RR = 3.2; 95% CI = 1.0–7.4). The increased risk of ovarian cancer was based on only 5 observed tumors and was found within the first 10 years after liver or biliary tract tumors.

Discussion

Persons with cancer of the liver and biliary tract were at a slightly lower risk of developing a second primary tumor than the population in general. However, survival is extremely short and on average only 1 year after diagnosis of the first primary. An increased risk of ovarian tumors was seen during the first 10 years of follow-up and could possibly be related to common etiologic factors, i.e., fat consumption might be associated with both gallbladder and ovarian cancers (*26*). However, none of the other possibly fat-related cancers (large bowel, breast, or corpus uteri) were found in excess, and metastases to the ovaries are frequent.

PANCREAS (ICD-7, 157)

Cancer of the pancreas accounts for 3.6% of all tumors in Danish men and 3.1% in women. The age-standardized incidence rate is 9.1 and 7.0/100,000 in men and women, respectively (*1*). Males are 1.3 times more likely to develop this disease than females. Incidence rates are only slightly higher in urban than in rural areas. During the period 1943–68, a constant increase in incidence was noted in both sexes, followed by a period of more stable rates (*27*). The observed increase in incidence must be ascribed at least partly to improved diagnostic methods. Only 28% of the pancreatic cancer cases were histologically verified in the 1940s compared with 77% today (*1, 3*). Risk factors for pancreatic cancer are to a large extent unknown, but tobacco smoking has been associated with a twofold to threefold increase (*28*). The absence of a substantial male excess and the lack of an urban-rural gradient in Denmark, which is consistently found for other tobacco-related cancers, add little support to the hypothesis that a major proportion of all pancreatic cancer in Denmark could be attributable to smoking habits. Other possible risk factors include coffee drinking and a high fat diet (*29, 30*).

Results

Altogether, 7,752 persons with cancer of the pancreas were registered by the Registry during 1943–80 and are included in the present study. The average age at diagnosis was 66 years, and the average follow-up was about 11 months. Only 3% of the persons with pancreatic cancer received radiotherapy as the initial course of treatment, whereas approximately 50% underwent surgery. A total of 88 second primary cancers were recorded. Both the first and the second primary cancers were histologically verified in only 52% of the cases, and only 57% of the initial pancreatic cancers were histologically confirmed.

Among men, the RR of developing a second tumor was 0.9 (95% CI = 0.6–1.2). This RR estimate was only marginally affected by the deduction of the expected numbers of pancreatic cancers. The only tumor site for which the excess was significant in men was the kidney (RR = 3.2; 95% CI = 1.0–7.5). Among women, 47 cases of second primary cancers were observed versus 37.2 expected (RR = 1.3; 95% CI = 0.9–1.7). This increased risk can primarily be ascribed to an excess of cancers of the female genital tract (RR = 2.6; 95% CI = 1.5–4.2), of which cancers of the corpus uteri (RR = 3.2) and ovary (RR = 3.1) were significantly elevated. An excess of second cancers was found among the 70 women surviving 10 or more years after the pancreatic cancer diagnosis (RR = 2.5; 95% CI = 1.4–4.0), attributable mainly to a significant excess of female genital cancers but also to colorectal tumors.

Discussion

The overall risk of cancer development following pancreatic cancer was not increased, although a 26% excess of second cancers in women was found, largely attributable to cancers of the female genital organs. A deficit of second cancers among men is only seen during the first 5 years of follow-up and may be ascribed to a possible reluctance of physicians to accept tumors of the digestive and respiratory system as truly new cancers (*10*). The excess of kidney cancer may be due to the special medical attention given to these retroperitoneal organs or possibly just to chance.

The most striking finding is the excess risk of cancers of the genital organs in women, particularly among long-term survivors. Except for cancer of the cervix uteri, all these sites were suggested to be associated with dietary fat intake, as has cancer of the pancreas (*29*). Among female long-term survivors, a total of 12 such "fat-related" cancers of the colon and rectum, breast, corpus uteri, and ovary were observed versus 3.3 expected (RR = 3.6; CI = 1.9–6.3). However, the initial diagnosis of pancreatic cancer must be doubted in patients surviving for 10 or more years with this highly fatal disease, and clarification of the association by special investigations is needed. In view of the reported association between tobacco smoking and pancreatic cancer (*28, 30*), it is noteworthy that the RR of lung cancer was only 0.5.

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ESOPHAGUS
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the esophagus, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,778	1,406	4,184
No. who developed a second primary cancer	33	22	55
Average age at diagnosis of first cancer, yr	68	71	69
Average yr of diagnosis of first cancer	1962	1962	1962
Person-yr of follow-up	3,106	1,990	5,096
Average follow-up, yr	1.1	1.4	1.2
Percent given radiotherapy for first cancer	50	50	50

[a] ICD-7 code = 150.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the esophagus in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	39	70.9
Only the first cancer	10	18.2
Only the second cancer	3	5.5
Neither first nor second cancer	3	5.5
Total second primary cancers	55	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

ESOPHAGUS
BOTH SEXES

TABLE 1C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the esophagus among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,184			1,069			205			87			4,184		
Person-yr in interval	2,361			1,520			683			532			5,096		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	17	28.81	0.6[b]	18	18.36	1.0	11	8.95	1.2	9	7.93	1.1	55	64.05	0.9
All excluding site of initial cancer	17	28.24	0.6[b]	18	18.06	1.0	11	8.82	1.2	9	7.83	1.1	55	62.94	0.9
Buccal cavity, pharynx	0	0.79	0.0	1	0.47	2.1	2	0.21	9.5[b]	0	0.18	0.0	3	1.65	1.8
Lip	0	0.38	0.0	0	0.22	0.0	1	0.10	10.0	0	0.08	0.0	1	0.77	1.3
Tongue	0	0.08	0.0	0	0.05	0.0	1	0.02	50.0	0	0.02	0.0	1	0.16	6.3
Salivary gland	0	0.08	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.17	0.0
Gum, other mouth	0	0.13	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.29	0.0
Pharynx	0	0.12	0.0	1	0.08	12.5	0	0.03	0.0	0	0.03	0.0	1	0.25	4.0
Digestive system	7	12.25	0.6	3	7.29	0.4	1	3.45	0.3	2	2.90	0.7	13	25.88	0.5[b]
Esophagus	0	0.57	0.0	0	0.30	0.0	0	0.13	0.0	0	0.10	0.0	0	1.11	0.0
Stomach	2	4.25	0.5	2	2.29	0.9	1	0.99	1.0	0	0.74	0.0	5	8.28	0.6
Colon	1	2.84	0.4	0	1.81	0.0	0	0.92	0.0	1	0.82	1.2	2	6.40	0.3
Rectum	2	2.46	0.8	1	1.47	0.7	0	0.68	0.0	0	0.58	0.0	3	5.20	0.6
Liver, biliary	1	0.64	1.6	0	0.46	0.0	0	0.24	0.0	0	0.22	0.0	1	1.56	0.6
Pancreas	1	1.01	1.0	0	0.69	0.0	0	0.35	0.0	1	0.33	3.0	2	2.40	0.8
Respiratory system	0	3.65	0.0	3	2.49	1.2	1	1.24	0.8	2	1.21	1.7	6	8.58	0.7
Nasal cavities, sinuses	0	0.08	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.16	0.0
Larynx	0	0.25	0.0	0	0.16	0.0	0	0.08	0.0	0	0.08	0.0	0	0.56	0.0
Trachea, bronchus, lung	0	3.10	0.0	3	2.15	1.4	1	1.07	0.9	2	1.06	1.9	6	7.39	0.8
Female breast	0	1.79	0.0	3	1.34	2.2	2	0.69	2.9	2	0.57	3.5	7	4.39	1.6
Female genital tract	1	1.41	0.7	2	1.08	1.8	0	0.55	0.0	1	0.47	2.1	4	3.51	1.1
Cervix uteri	0	0.39	0.0	2	0.29	6.8	0	0.14	0.0	1	0.11	8.9	3	0.94	3.2
Corpus uteri	0	0.40	0.0	0	0.32	0.0	0	0.17	0.0	0	0.14	0.0	0	1.03	0.0
Uterus, NOS	0	0.06	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.12	0.0
Ovary, fallopian tubes	0	0.43	0.0	0	0.34	0.0	0	0.18	0.0	0	0.16	0.0	0	1.11	0.0
Prostate gland	1	2.65	0.4	2	1.58	1.3	3	0.77	3.9	1	0.76	1.3	7	5.77	1.2
Testis	0	0.06	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.12	0.0
Kidney, renal pelvis, ureter	5	0.82	6.1[b]	0	0.55	0.0	0	0.28	0.0	0	0.24	0.0	5	1.89	2.6
Bladder, other urinary	2	1.64	1.2	0	1.09	0.0	1	0.54	1.9	0	0.54	0.0	3	3.81	0.8
Melanoma of the skin	0	0.23	0.0	0	0.17	0.0	0	0.08	0.0	0	0.07	0.0	0	0.54	0.0
Eye	0	0.08	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.18	0.0
Brain, central nervous system	0	0.38	0.0	0	0.27	0.0	0	0.14	0.0	0	0.12	0.0	0	0.91	0.0
Thyroid gland	0	0.12	0.0	0	0.08	0.0	0	0.05	0.0	0	0.03	0.0	0	0.27	0.0
Bone	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.11	0.0
Connective tissue	0	0.10	0.0	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	0	0.21	0.0
Lymphatic, hematopoietic system	0	1.62	0.0	1	1.08	0.9	1	0.54	1.9	1	0.50	2.0	3	3.74	0.8
Non-Hodgkin's lymphoma	0	0.43	0.0	0	0.29	0.0	1	0.15	6.7	0	0.13	0.0	1	1.00	1.0
Hodgkin's disease	0	0.11	0.0	0	0.07	0.0	0	0.03	0.0	1	0.03	33.3	1	0.24	4.2
Multiple myeloma	0	0.30	0.0	0	0.21	0.0	0	0.10	0.0	0	0.10	0.0	0	0.71	0.0
Leukemias	0	0.77	0.0	1	0.50	2.0	0	0.25	0.0	0	0.22	0.0	1	1.75	0.6
Chronic lymphocytic	0	0.43	0.0	1	0.28	3.6	0	0.13	0.0	0	0.12	0.0	1	0.95	1.1
Acute nonlymphocytic	0	0.16	0.0	0	0.11	0.0	0	0.06	0.0	0	0.06	0.0	0	0.40	0.0

[a] ICD-7 code = 150.

[b] $P < .05$.

ESOPHAGUS MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the esophagus among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5– yr			10+ yr			Total		
No. starting interval	2,778			666			116			48			2,778		
Person-yr in interval	1,529			903			383			291			3,106		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**13**	**19.24**	**0.7**	**10**	**11.41**	**0.9**	**7**	**5.34**	**1.3**	**3**	**4.93**	**0.6**	**33**	**40.92**	**0.8**
All excluding site of initial cancer	**13**	**18.81**	**0.7**	**10**	**11.19**	**0.9**	**7**	**5.25**	**1.3**	**3**	**4.86**	**0.6**	**33**	**40.11**	**0.8**
Buccal cavity, pharynx	**0**	**0.65**	**0.0**	**1**	**0.37**	**2.7**	**1**	**0.16**	**6.2**	**0**	**0.14**	**0.0**	**2**	**1.32**	**1.5**
Lip	0	0.36	0.0	0	0.20	0.0	1	0.09	11.3	0	0.07	0.0	1	0.72	1.4
Tongue	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Salivary gland	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.11	0.0
Gum, other mouth	0	0.09	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.19	0.0
Pharynx	0	0.10	0.0	1	0.06	17.5	0	0.02	0.0	0	0.02	0.0	1	0.20	4.9
Digestive system	**5**	**8.25**	**0.6**	**3**	**4.55**	**0.7**	**1**	**2.04**	**0.5**	**0**	**1.75**	**0.0**	**9**	**16.58**	**0.5**
Esophagus	0	0.43	0.0	0	0.22	0.0	0	0.09	0.0	0	0.07	0.0	0	0.81	0.0
Stomach	2	2.97	0.7	2	1.52	1.3	1	0.63	1.6	0	0.48	0.0	5	5.61	0.9
Colon	0	1.72	0.0	0	0.99	0.0	0	0.48	0.0	0	0.44	0.0	0	3.63	0.0
Rectum	2	1.81	1.1	1	1.01	1.0	0	0.45	0.0	0	0.39	0.0	3	3.66	0.8
Liver, biliary	0	0.35	0.0	0	0.23	0.0	0	0.11	0.0	0	0.11	0.0	0	0.80	0.0
Pancreas	1	0.68	1.5	0	0.43	0.0	0	0.21	0.0	0	0.20	0.0	1	1.54	0.7
Respiratory system	**0**	**3.22**	**0.0**	**2**	**2.15**	**0.9**	**1**	**1.06**	**0.9**	**2**	**1.05**	**1.9**	**5**	**7.47**	**0.7**
Nasal cavities, sinuses	0	0.06	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.12	0.0
Larynx	0	0.23	0.0	0	0.15	0.0	0	0.07	0.0	0	0.07	0.0	0	0.52	0.0
Trachea, bronchus, lung	0	2.76	0.0	2	1.87	1.1	1	0.92	1.1	2	0.92	2.2	5	6.47	0.8
Prostate gland	1	2.65	0.4	2	1.58	1.3	3	0.77	3.9	1	0.76	1.3	7	5.77	1.2
Testis	0	0.06	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.12	0.0
Kidney, renal pelvis, ureter	5	0.58	8.7[b]	0	0.36	0.0	0	0.18	0.0	0	0.16	0.0	5	1.28	3.9[b]
Bladder, other urinary	2	1.38	1.4	0	0.89	0.0	1	0.43	2.3	0	0.44	0.0	3	3.14	1.0
Melanoma of the skin	0	0.14	0.0	0	0.09	0.0	0	0.04	0.0	0	0.04	0.0	0	0.30	0.0
Eye	0	0.06	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.12	0.0
Brain, central nervous system	0	0.25	0.0	0	0.17	0.0	0	0.08	0.0	0	0.07	0.0	0	0.57	0.0
Thyroid gland	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.11	0.0
Bone	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Connective tissue	0	0.07	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.14	0.0
Lymphatic, hematopoietic system	**0**	**1.15**	**0.0**	**0**	**0.71**	**0.0**	**0**	**0.34**	**0.0**	**0**	**0.32**	**0.0**	**0**	**2.52**	**0.0**
Non-Hodgkin's lymphoma	0	0.29	0.0	0	0.18	0.0	0	0.09	0.0	0	0.08	0.0	0	0.64	0.0
Hodgkin's disease	0	0.08	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.17	0.0
Multiple myeloma	0	0.21	0.0	0	0.13	0.0	0	0.06	0.0	0	0.06	0.0	0	0.46	0.0
Leukemias	0	0.56	0.0	0	0.34	0.0	0	0.16	0.0	0	0.15	0.0	0	1.22	0.0
Chronic lymphocytic	0	0.33	0.0	0	0.20	0.0	0	0.09	0.0	0	0.09	0.0	0	0.70	0.0
Acute nonlymphocytic	0	0.11	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.26	0.0

[a] ICD-7 code = 150.

[b] $P < .05$.

ESOPHAGUS
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the esophagus among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,406			403			89			39			1,406		
Person-yr in interval	832			617			300			241			1,990		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**9.57**	**0.4**	**8**	**6.95**	**1.2**	**4**	**3.61**	**1.1**	**6**	**3.00**	**2.0**	**22**	**23.13**	**1.0**
All excluding site of initial cancer	**4**	**9.43**	**0.4**	**8**	**6.87**	**1.2**	**4**	**3.57**	**1.1**	**6**	**2.97**	**2.0**	**22**	**22.83**	**1.0**
Buccal cavity, pharynx	**0**	**0.14**	**0.0**	**0**	**0.10**	**0.0**	**1**	**0.05**	**19.6**	**0**	**0.04**	**0.0**	**1**	**0.33**	**3.0**
Lip	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Tongue	0	0.03	0.0	0	0.02	0.0	1	0.01	103.6[b]	0	0.01	0.0	1	0.06	15.7
Salivary gland	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Gum, other mouth	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.10	0.0
Pharynx	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Digestive system	**2**	**4.00**	**0.5**	**0**	**2.74**	**0.0**	**0**	**1.41**	**0.0**	**2**	**1.15**	**1.7**	**4**	**9.30**	**0.4**
Esophagus	0	0.14	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.30	0.0
Stomach	0	1.28	0.0	0	0.77	0.0	0	0.36	0.0	0	0.26	0.0	0	2.67	0.0
Colon	1	1.12	0.9	0	0.82	0.0	0	0.44	0.0	1	0.38	2.6	2	2.77	0.7
Rectum	0	0.65	0.0	0	0.46	0.0	0	0.23	0.0	0	0.19	0.0	0	1.54	0.0
Liver, biliary	1	0.29	3.4	0	0.23	0.0	0	0.13	0.0	0	0.11	0.0	1	0.76	1.3
Pancreas	0	0.33	0.0	0	0.26	0.0	0	0.14	0.0	1	0.13	7.7	1	0.86	1.2
Respiratory system	**0**	**0.43**	**0.0**	**1**	**0.34**	**2.9**	**0**	**0.18**	**0.0**	**0**	**0.16**	**0.0**	**1**	**1.11**	**0.9**
Nasal cavities, sinuses	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.04	0.0
Larynx	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Trachea, bronchus, lung	0	0.34	0.0	1	0.28	3.5	0	0.15	0.0	0	0.14	0.0	1	0.92	1.1
Female breast	0	1.79	0.0	3	1.34	2.2	2	0.69	2.9	2	0.57	3.5	7	4.39	1.6
Female genital tract	**1**	**1.41**	**0.7**	**2**	**1.08**	**1.8**	**0**	**0.55**	**0.0**	**1**	**0.47**	**2.1**	**4**	**3.51**	**1.1**
Cervix uteri	0	0.39	0.0	2	0.29	6.8	0	0.14	0.0	1	0.11	8.9	3	0.94	3.2
Corpus uteri	0	0.40	0.0	0	0.32	0.0	0	0.17	0.0	0	0.14	0.0	0	1.03	0.0
Uterus, NOS	0	0.06	0.0	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.12	0.0
Ovary, fallopian tubes	0	0.43	0.0	0	0.34	0.0	0	0.18	0.0	0	0.16	0.0	0	1.11	0.0
Kidney, renal pelvis, ureter	0	0.24	0.0	0	0.19	0.0	0	0.10	0.0	0	0.08	0.0	0	0.61	0.0
Bladder, other urinary	0	0.26	0.0	0	0.20	0.0	0	0.11	0.0	0	0.10	0.0	0	0.67	0.0
Melanoma of the skin	0	0.09	0.0	0	0.08	0.0	0	0.04	0.0	0	0.03	0.0	0	0.24	0.0
Eye	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Brain, central nervous system	0	0.13	0.0	0	0.10	0.0	0	0.06	0.0	0	0.05	0.0	0	0.34	0.0
Thyroid gland	0	0.07	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.16	0.0
Bone	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.00	0.0	0	0.04	0.0
Connective tissue	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Lymphatic, hematopoietic system	**0**	**0.47**	**0.0**	**1**	**0.37**	**2.7**	**1**	**0.20**	**5.0**	**1**	**0.18**	**5.6**	**3**	**1.22**	**2.4**
Non-Hodgkin's lymphoma	0	0.14	0.0	0	0.11	0.0	1	0.06	16.5	0	0.05	0.0	1	0.36	2.8
Hodgkin's disease	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	1	0.01	102.0[b]	1	0.07	13.5
Multiple myeloma	0	0.09	0.0	0	0.08	0.0	0	0.04	0.0	0	0.04	0.0	0	0.25	0.0
Leukemias	0	0.21	0.0	1	0.16	6.3	0	0.09	0.0	0	0.07	0.0	1	0.53	1.9
Chronic lymphocytic	0	0.10	0.0	1	0.08	13.2	0	0.04	0.0	0	0.03	0.0	1	0.25	4.0
Acute nonlymphocytic	0	0.05	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.14	0.0

[a] ICD-7 code = 150.

[b] $P < .05$.

STOMACH
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the stomach, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	18,442	12,401	30,843
No. who developed a second primary cancer	321	202	523
Average age at diagnosis of first cancer, yr	67	70	68
Average yr of diagnosis of first cancer	1960	1960	1960
Person-yr of follow-up	34,997	21,908	56,905
Average follow-up, yr	1.9	1.8	1.9
Percent given radiotherapy for first cancer	4	3	4

[a] ICD-7 code = 151.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the stomach in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	385	73.6
Only the first cancer	70	13.4
Only the second cancer	37	7.1
Neither first nor second cancer	31	5.9
Total second primary cancers	523	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

STOMACH
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the stomach among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	30,843			9,656			2,844			1,453			30,843		
Person-yr in interval	17,869			18,603			10,077			10,356			56,905		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**96**	**206.88**	**0.5**[b]	**167**	**219.28**	**0.8**[b]	**136**	**138.59**	**1.0**	**124**	**172.03**	**0.7**[b]	**523**	**736.79**	**0.7**[b]
All excluding site of initial cancer	**96**	**176.75**	**0.5**[b]	**165**	**191.23**	**0.9**	**136**	**121.59**	**1.1**	**124**	**153.52**	**0.8**[b]	**521**	**643.09**	**0.8**[b]
Buccal cavity, pharynx	**1**	**5.52**	**0.2**	**4**	**5.65**	**0.7**	**5**	**3.41**	**1.5**	**1**	**3.95**	**0.3**	**11**	**18.52**	**0.6**
Lip	0	2.63	0.0	1	2.70	0.4	1	1.61	0.6	1	1.81	0.6	3	8.76	0.3
Tongue	0	0.56	0.0	0	0.56	0.0	0	0.34	0.0	0	0.37	0.0	0	1.82	0.0
Salivary gland	1	0.58	1.7	0	0.61	0.0	0	0.37	0.0	0	0.40	0.0	1	1.97	0.5
Gum, other mouth	0	0.88	0.0	1	0.91	1.1	1	0.59	1.7	0	0.78	0.0	2	3.16	0.6
Pharynx	0	0.87	0.0	2	0.86	2.3	3	0.50	6.0[b]	0	0.58	0.0	5	2.81	1.8
Digestive system	**36**	**86.80**	**0.4**[b]	**57**	**87.47**	**0.7**[b]	**46**	**55.23**	**0.8**	**49**	**66.66**	**0.7**[b]	**188**	**296.16**	**0.6**[b]
Esophagus	1	3.74	0.3	2	3.50	0.6	1	2.13	0.5	2	2.44	0.8	6	11.81	0.5
Stomach	0	30.13	0.0[b]	2	28.05	0.1[b]	0	17.00	0.0[b]	0	18.51	0.0[b]	2	93.70	0.0[b]
Colon	13	20.18	0.6	26	21.47	1.2	21	14.15	1.5	17	18.51	0.9	77	74.32	1.0
Rectum	8	17.44	0.5[b]	13	17.75	0.7	7	11.10	0.6	15	13.20	1.1	43	59.49	0.7[b]
Liver, biliary	5	4.66	1.1	2	5.32	0.4	3	3.58	0.8	3	4.83	0.6	13	18.40	0.7
Pancreas	8	7.30	1.1	8	8.29	1.0	13	5.46	2.4[b]	10	7.20	1.4	39	28.26	1.4
Respiratory system	**6**	**25.42**	**0.2**[b]	**26**	**29.72**	**0.9**	**18**	**18.69**	**1.0**	**15**	**24.25**	**0.6**	**65**	**98.09**	**0.7**[b]
Nasal cavities, sinuses	0	0.50	0.0	1	0.50	2.0	0	0.31	0.0	1	0.37	2.7	2	1.68	1.2
Larynx	0	1.69	0.0	0	1.90	0.0	1	1.16	0.9	2	1.45	1.4	3	6.20	0.5
Trachea, bronchus, lung	4	21.66	0.2[b]	25	25.60	1.0	17	16.12	1.1	10	21.08	0.5[b]	56	84.45	0.7[b]
Female breast	5	14.05	0.4[b]	13	14.72	0.9	8	8.88	0.9	11	10.53	1.0	37	48.18	0.8
Female genital tract	**18**	**11.42**	**1.6**	**19**	**12.09**	**1.6**	**8**	**6.90**	**1.2**	**11**	**7.65**	**1.4**	**56**	**38.06**	**1.5**[b]
Cervix uteri	2	3.36	0.6	4	3.47	1.2	5	1.83	2.7	4	1.84	2.2	15	10.50	1.4
Corpus uteri	3	3.15	1.0	2	3.44	0.6	1	1.99	0.5	6	2.24	2.7	12	10.82	1.1
Uterus, NOS	1	0.47	2.1	2	0.41	4.9	1	0.24	4.2	0	0.26	0.0	4	1.38	2.9
Ovary, fallopian tubes	10	3.45	2.9[b]	11	3.76	2.9[b]	1	2.20	0.5	1	2.54	0.4	23	11.95	1.9[b]
Prostate gland	10	18.66	0.5[b]	17	20.44	0.8	16	14.20	1.1	14	19.36	0.7	57	72.65	0.8
Testis	0	0.40	0.0	0	0.43	0.0	0	0.22	0.0	2	0.23	8.6	2	1.28	1.6
Kidney, renal pelvis, ureter	1	5.83	0.2[b]	6	6.48	0.9	5	4.15	1.2	0	5.31	0.0[b]	12	21.75	0.6[b]
Bladder, other urinary	8	11.48	0.7	8	13.05	0.6	14	8.58	1.6	12	11.54	1.0	42	44.64	0.9
Melanoma of the skin	1	1.62	0.6	0	1.83	0.0	1	1.14	0.9	1	1.45	0.7	3	6.05	0.5
Eye	0	0.60	0.0	1	0.64	1.6	0	0.38	0.0	0	0.43	0.0	1	2.05	0.5
Brain, central nervous system	3	2.82	1.1	2	3.19	0.6	0	1.82	0.0	0	2.06	0.0	5	9.88	0.5
Thyroid gland	1	0.87	1.1	1	0.94	1.1	1	0.59	1.7	0	0.73	0.0	3	3.14	1.0
Bone	0	0.39	0.0	0	0.40	0.0	1	0.24	4.2	0	0.27	0.0	1	1.31	0.8
Connective tissue	0	0.76	0.0	0	0.76	0.0	0	0.44	0.0	1	0.48	2.1	1	2.43	0.4
Lymphatic, hematopoietic system	**4**	**11.81**	**0.3**[b]	**12**	**13.23**	**0.9**	**11**	**8.51**	**1.3**	**7**	**10.81**	**0.6**	**34**	**44.36**	**0.8**
Non-Hodgkin's lymphoma	0	3.09	0.0	4	3.46	1.2	3	2.22	1.4	1	2.83	0.4	8	11.60	0.7
Hodgkin's disease	0	0.79	0.0	0	0.87	0.0	0	0.52	0.0	1	0.59	1.7	1	2.77	0.4
Multiple myeloma	0	2.22	0.0	2	2.56	0.8	3	1.67	1.8	1	2.15	0.5	6	8.59	0.7
Leukemias	4	5.60	0.7	6	6.21	1.0	5	4.03	1.2	3	5.15	0.6	18	20.98	0.9
Chronic lymphocytic	2	3.11	0.6	3	3.41	0.9	3	2.24	1.3	1	2.86	0.3	9	11.63	0.8
Acute nonlymphocytic	0	1.13	0.0	2	1.35	1.5	1	0.92	1.1	0	1.27	0.0	3	4.66	0.6

[a] ICD-7 code = 151.

[b] $P < .05$.

STOMACH
MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the stomach among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	18,442			6,050			1,763			895			18,442		
Person-yr in interval	10,931			11,540			6,222			6,304			34,997		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**53**	**132.64**	**0.4[b]**	**99**	**142.87**	**0.7[b]**	**90**	**91.56**	**1.0**	**79**	**116.09**	**0.7[b]**	**321**	**483.16**	**0.7[b]**
All excluding site of initial cancer	**53**	**112.57**	**0.5[b]**	**98**	**123.70**	**0.8[b]**	**90**	**79.87**	**1.1**	**79**	**103.23**	**0.8[b]**	**320**	**419.36**	**0.8[b]**
Buccal cavity, pharynx	**0**	**4.44**	**0.0[b]**	**3**	**4.56**	**0.7**	**4**	**2.73**	**1.5**	**1**	**3.14**	**0.3**	**8**	**14.87**	**0.5**
Lip	0	2.47	0.0	1	2.53	0.4	1	1.51	0.7	1	1.69	0.6	3	8.20	0.4
Tongue	0	0.34	0.0	0	0.35	0.0	0	0.21	0.0	0	0.22	0.0	0	1.11	0.0
Salivary gland	0	0.36	0.0	0	0.38	0.0	0	0.23	0.0	0	0.26	0.0	0	1.24	0.0
Gum, other mouth	0	0.59	0.0	1	0.61	1.6	0	0.39	0.0	0	0.50	0.0	1	2.09	0.5
Pharynx	0	0.68	0.0	1	0.68	1.5	3	0.40	7.5[b]	0	0.46	0.0	4	2.22	1.8
Digestive system	**23**	**56.14**	**0.4[b]**	**35**	**57.15**	**0.6[b]**	**31**	**36.15**	**0.9**	**34**	**43.88**	**0.8**	**123**	**193.32**	**0.6[b]**
Esophagus	1	2.73	0.4	2	2.57	0.8	0	1.54	0.0	1	1.74	0.6	4	8.58	0.5
Stomach	0	20.07	0.0[b]	1	19.17	0.1[b]	0	11.69	0.0[b]	0	12.86	0.0[b]	1	63.80	0.0[b]
Colon	7	11.78	0.6	16	12.58	1.3	13	8.35	1.6	12	11.11	1.1	48	43.82	1.1
Rectum	5	12.40	0.4[b]	8	12.70	0.6	6	7.96	0.8	10	9.52	1.1	29	42.59	0.7[b]
Liver, biliary	3	2.49	1.2	0	2.86	0.0	3	1.94	1.5	3	2.68	1.1	9	9.97	0.9
Pancreas	6	4.84	1.2	6	5.51	1.1	9	3.62	2.5[b]	6	4.78	1.3	27	18.76	1.4
Respiratory system	**5**	**22.29**	**0.2[b]**	**22**	**26.22**	**0.8**	**17**	**16.46**	**1.0**	**13**	**21.37**	**0.6**	**57**	**86.34**	**0.7[b]**
Nasal cavities, sinuses	0	0.38	0.0	1	0.39	2.5	0	0.24	0.0	1	0.29	3.5	2	1.30	1.5
Larynx	0	1.56	0.0	0	1.77	0.0	1	1.08	0.9	2	1.35	1.5	3	5.76	0.5
Trachea, bronchus, lung	3	19.16	0.2[b]	21	22.73	0.9	16	14.27	1.1	8	18.65	0.4[b]	48	74.80	0.6[b]
Prostate gland	10	18.66	0.5[b]	17	20.44	0.8	16	14.20	1.1	14	19.36	0.7	57	72.65	0.8
Testis	0	0.40	0.0	0	0.43	0.0	0	0.22	0.0	2	0.23	8.6	2	1.28	1.6
Kidney, renal pelvis, ureter	0	4.01	0.0[b]	2	4.50	0.4	3	2.90	1.0	0	3.77	0.0[b]	5	15.17	0.3[b]
Bladder, other urinary	6	9.52	0.6	7	10.89	0.6	11	7.17	1.5	11	9.73	1.1	35	37.31	0.9
Melanoma of the skin	0	0.92	0.0	0	1.04	0.0	0	0.65	0.0	0	0.83	0.0	0	3.45	0.0
Eye	0	0.41	0.0	1	0.43	2.3	0	0.26	0.0	0	0.30	0.0	1	1.40	0.7
Brain, central nervous system	3	1.80	1.7	1	2.06	0.5	0	1.16	0.0	0	1.29	0.0	4	6.31	0.6
Thyroid gland	0	0.36	0.0	0	0.40	0.0	0	0.25	0.0	0	0.31	0.0	0	1.33	0.0
Bone	0	0.26	0.0	0	0.27	0.0	0	0.16	0.0	0	0.18	0.0	0	0.88	0.0
Connective tissue	0	0.51	0.0	0	0.51	0.0	0	0.30	0.0	1	0.33	3.0	1	1.65	0.6
Lymphatic, hematopoietic system	**4**	**8.19**	**0.5**	**11**	**9.19**	**1.2**	**6**	**5.91**	**1.0**	**3**	**7.55**	**0.4**	**24**	**30.84**	**0.8**
Non-Hodgkin's lymphoma	0	2.03	0.0	4	2.29	1.7	2	1.46	1.4	0	1.86	0.0	6	7.64	0.8
Hodgkin's disease	0	0.56	0.0	0	0.62	0.0	0	0.37	0.0	1	0.41	2.4	1	1.96	0.5
Multiple myeloma	0	1.50	0.0	2	1.73	1.2	2	1.13	1.8	1	1.47	0.7	5	5.82	0.9
Leukemias	4	4.02	1.0	5	4.46	1.1	2	2.90	0.7	1	3.74	0.3	12	15.12	0.8
Chronic lymphocytic	2	2.34	0.9	3	2.57	1.2	1	1.68	0.6	1	2.16	0.5	7	8.75	0.8
Acute nonlymphocytic	0	0.78	0.0	1	0.93	1.1	1	0.64	1.6	0	0.89	0.0	2	3.24	0.6

[a] ICD-7 code = 151.
[b] $P < .05$.

STOMACH
FEMALES

TABLE 2E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the stomach among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	12,401			3,606			1,081			558			12,401		
Person-yr in interval	6,938			7,063			3,855			4,052			21,908		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**43**	**74.24**	**0.6**[b]	**68**	**76.41**	**0.9**	**46**	**47.03**	**1.0**	**45**	**55.94**	**0.8**	**202**	**253.63**	**0.8**[b]
All excluding site of initial cancer	**43**	**64.18**	**0.7**[b]	67	**67.53**	**1.0**	**46**	**41.72**	**1.1**	**45**	**50.29**	**0.9**	**201**	**223.73**	**0.9**
Buccal cavity, pharynx	**1**	**1.08**	**0.9**	**1**	**1.09**	**0.9**	**1**	**0.68**	**1.5**	**0**	**0.81**	**0.0**	**3**	**3.65**	**0.8**
Lip	0	0.16	0.0	0	0.17	0.0	0	0.10	0.0	0	0.12	0.0	0	0.56	0.0
Tongue	0	0.22	0.0	0	0.21	0.0	0	0.13	0.0	0	0.15	0.0	0	0.71	0.0
Salivary gland	1	0.22	4.5	0	0.23	0.0	0	0.14	0.0	0	0.14	0.0	1	0.73	1.4
Gum, other mouth	0	0.29	0.0	0	0.30	0.0	1	0.20	4.9	0	0.28	0.0	1	1.07	0.9
Pharynx	0	0.19	0.0	1	0.18	5.5	0	0.10	0.0	0	0.12	0.0	1	0.59	1.7
Digestive system	**13**	**30.66**	**0.4**[b]	**22**	**30.32**	**0.7**	**15**	**19.08**	**0.8**	**15**	**22.78**	**0.7**	**65**	**102.84**	**0.6**[b]
Esophagus	0	1.01	0.0	0	0.93	0.0	1	0.59	1.7	1	0.70	1.4	2	3.23	0.6
Stomach	0	10.06	0.0[b]	1	8.88	0.1[b]	0	5.31	0.0[b]	0	5.65	0.0[b]	1	29.90	0.0[b]
Colon	6	8.40	0.7	10	8.89	1.1	8	5.80	1.4	5	7.40	0.7	29	30.50	1.0
Rectum	3	5.04	0.6	5	5.05	1.0	1	3.14	0.3	5	3.68	1.4	14	16.90	0.8
Liver, biliary	2	2.17	0.9	2	2.46	0.8	0	1.64	0.0	0	2.15	0.0	4	8.43	0.5
Pancreas	2	2.46	0.8	2	2.78	0.7	4	1.84	2.2	4	2.42	1.7	12	9.50	1.3
Respiratory system	**1**	**3.13**	**0.3**	**4**	**3.50**	**1.1**	**1**	**2.23**	**0.4**	**2**	**2.88**	**0.7**	**8**	**11.75**	**0.7**
Nasal cavities, sinuses	0	0.12	0.0	0	0.11	0.0	0	0.07	0.0	0	0.08	0.0	0	0.38	0.0
Larynx	0	0.13	0.0	0	0.13	0.0	0	0.08	0.0	0	0.10	0.0	0	0.44	0.0
Trachea, bronchus, lung	1	2.50	0.4	4	2.87	1.4	1	1.85	0.5	2	2.43	0.8	8	9.65	0.8
Female breast	5	14.05	0.4[b]	13	14.72	0.9	8	8.88	0.9	11	10.53	1.0	37	48.18	0.8
Female genital tract	**18**	**11.42**	**1.6**	**19**	**12.09**	**1.6**	**8**	**6.90**	**1.2**	**11**	**7.65**	**1.4**	**56**	**38.06**	**1.5**[b]
Cervix uteri	2	3.36	0.6	4	3.47	1.2	5	1.83	2.7	4	1.84	2.2	15	10.50	1.4
Corpus uteri	3	3.15	1.0	2	3.44	0.6	1	1.99	0.5	6	2.24	2.7	12	10.82	1.1
Uterus, NOS	1	0.47	2.1	2	0.41	4.9	1	0.24	4.2	0	0.26	0.0	4	1.38	2.9
Ovary, fallopian tubes	10	3.45	2.9[b]	11	3.76	2.9[b]	1	2.20	0.5	1	2.54	0.4	23	11.95	1.9[b]
Kidney, renal pelvis, ureter	1	1.82	0.6	4	1.98	2.0	2	1.25	1.6	0	1.54	0.0	7	6.58	1.1
Bladder, other urinary	2	1.96	1.0	1	2.16	0.5	3	1.41	2.1	1	1.81	0.6	7	7.33	1.0
Melanoma of the skin	1	0.70	1.4	0	0.79	0.0	1	0.49	2.0	1	0.62	1.6	3	2.60	1.2
Eye	0	0.19	0.0	0	0.21	0.0	0	0.12	0.0	0	0.13	0.0	0	0.65	0.0
Brain, central nervous system	0	1.02	0.0	1	1.13	0.9	0	0.66	0.0	0	0.77	0.0	1	3.57	0.3
Thyroid gland	1	0.51	1.9	1	0.54	1.8	1	0.34	2.9	0	0.42	0.0	3	1.81	1.7
Bone	0	0.13	0.0	0	0.13	0.0	1	0.08	13.0	0	0.09	0.0	1	0.43	2.3
Connective tissue	0	0.25	0.0	0	0.25	0.0	0	0.14	0.0	0	0.15	0.0	0	0.78	0.0
Lymphatic, hematopoietic system	**0**	**3.62**	**0.0**	**1**	**4.04**	**0.2**	**5**	**2.60**	**1.9**	**4**	**3.26**	**1.2**	**10**	**13.52**	**0.7**
Non-Hodgkin's lymphoma	0	1.06	0.0	0	1.17	0.0	1	0.76	1.3	1	0.97	1.0	2	3.96	0.5
Hodgkin's disease	0	0.23	0.0	0	0.25	0.0	0	0.15	0.0	0	0.18	0.0	0	0.81	0.0
Multiple myeloma	0	0.72	0.0	0	0.83	0.0	1	0.54	1.9	0	0.68	0.0	1	2.77	0.4
Leukemias	0	1.58	0.0	1	1.75	0.6	3	1.13	2.7	2	1.41	1.4	6	5.86	1.0
Chronic lymphocytic	0	0.77	0.0	0	0.84	0.0	2	0.56	3.6	0	0.70	0.0	2	2.88	0.7
Acute nonlymphocytic	0	0.35	0.0	1	0.42	2.4	0	0.28	0.0	0	0.38	0.0	1	1.42	0.7

[a] ICD-7 code = 151.

[b] $P < .05$.

SMALL INTESTINE
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the small intestine, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	467	401	868
No. who developed a second primary cancer	20	16	36
Average age at diagnosis of first cancer, yr	63	63	63
Average yr of diagnosis of first cancer	1966	1965	1966
Person-yr of follow-up	1,328	1,232	2,560
Average follow-up, yr	2.8	3.0	2.9
Percent given radiotherapy for first cancer	6	5	6

[a] ICD-7 code = 152.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the small intestine in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	29	80.6
Only the first cancer	4	11.1
Only the second cancer	2	5.6
Neither first nor second cancer	1	2.8
Total second primary cancers	36	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

SMALL INTESTINE
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the small intestine among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	868			414			152			63			868		
Person-yr in interval	597			941			504			518			2,560		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	7	5.64	1.2	11	8.87	1.2	11	5.25	2.1^b	7	7.06	1.0	36	26.83	1.3
All excluding site of initial cancer	7	5.62	1.2	11	8.84	1.2	11	5.23	2.1^b	7	7.04	1.0	36	26.75	1.3
Buccal cavity, pharynx	0	0.14	0.0	0	0.22	0.0	0	0.12	0.0	0	0.15	0.0	0	0.63	0.0
Lip	0	0.07	0.0	0	0.10	0.0	0	0.05	0.0	0	0.07	0.0	0	0.28	0.0
Tongue	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Salivary gland	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Gum, other mouth	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.12	0.0
Pharynx	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.11	0.0
Digestive system	2	2.04	1.0	6	3.04	2.0	2	1.86	1.1	6	2.59	2.3	16	9.52	1.7
Esophagus	0	0.07	0.0	0	0.11	0.0	0	0.07	0.0	0	0.09	0.0	0	0.35	0.0
Stomach	0	0.58	0.0	0	0.81	0.0	0	0.49	0.0	0	0.64	0.0	0	2.53	0.0
Colon	0	0.54	0.0	1	0.82	1.2	1	0.51	2.0	3	0.77	3.9	5	2.65	1.9
Rectum	0	0.42	0.0	2	0.63	3.2	1	0.38	2.6	1	0.51	2.0	4	1.93	2.1
Liver, biliary	1	0.14	7.1	3	0.22	13.6^b	0	0.14	0.0	0	0.21	0.0	4	0.70	5.7^b
Pancreas	1	0.21	4.8	0	0.34	0.0	0	0.21	0.0	2	0.30	6.7	3	1.05	2.9
Respiratory system	3	0.80	3.8	0	1.36	0.0	2	0.78	2.6	0	0.97	0.0	5	3.91	1.3
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Larynx	2	0.06	33.3^b	0	0.09	0.0	0	0.04	0,0	0	0.06	0.0	2	0.25	8.0
Trachea, bronchus, lung	1	0.70	1.4	0	1.19	0.0	2	0.68	2.9	0	0.85	0.0	3	3.42	0.9
Female breast	0	0.51	0.0	1	0.77	1.3	1	0.45	2.2	0	0.59	0.0	2	2.32	0.9
Female genital tract	1	0.45	2.2	2	0.73	2.7	1	0.40	2.5	0	0.47	0.0	4	2.05	2.0
Cervix uteri	0	0.15	0.0	0	0.24	0.0	0	0.12	0.0	0	0.13	0.0	0	0.63	0.0
Corpus uteri	0	0.13	0.0	1	0.22	4.6	0	0.12	0.0	0	0.14	0.0	1	0.61	1.6
Uterus, NOS	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Ovary, fallopian tubes	1	0.14	7.3	1	0.22	4.6	1	0.12	8.1	0	0.15	0.0	3	0.63	4.8
Prostate gland	0	0.41	0.0	1	0.69	1.5	3	0.42	7.2^b	1	0.67	1.5	5	2.18	2.3
Testis	0	0.02	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Kidney, renal pelvis, ureter	0	0.17	0.0	0	0.28	0.0	0	0.16	0.0	0	0.22	0.0	0	0.83	0.0
Bladder, other urinary	1	0.33	3.0	1	0.55	1.8	1	0.33	3.0	0	0.46	0.0	3	1.67	1.8
Melanoma of the skin	0	0.06	0.0	0	0.11	0.0	0	0.06	0.0	0	0.07	0.0	0	0.30	0.0
Eye	0	0.02	0.0	0	0.03	0.0	1	0.02	50.0	0	0.02	0.0	1	0.08	12.5
Brain, central nervous system	0	0.11	0.0	0	0.18	0.0	0	0.09	0.0	0	0.10	0.0	0	0.48	0.0
Thyroid gland	0	0.03	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.12	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Lymphatic, hematopoietic system	0	0.34	0.0	0	0.54	0.0	0	0.33	0.0	0	0.44	0.0	0	1.65	0.0
Non-Hodgkin's lymphoma	0	0.09	0.0	0	0.15	0.0	0	0.09	0.0	0	0.12	0.0	0	0.46	0.0
Hodgkin's disease	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.11	0.0
Multiple myeloma	0	0.07	0.0	0	0.11	0.0	0	0.07	0.0	0	0.09	0.0	0	0.31	0.0
Leukemias	0	0.15	0.0	0	0.24	0.0	0	0.14	0.0	0	0.21	0.0	0	0.75	0.0
Chronic lymphocytic	0	0.07	0.0	0	0.12	0.0	0	0.07	0.0	0	0.12	0.0	0	0.39	0.0
Acute nonlymphocytic	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.05	0.0	0	0.20	0.0

[a] ICD-7 code = 152.

[b] $P < .05$.

COLON
BOTH SEXES

TABLE 4A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the colon or rectosigmoid junction, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	13,093	16,397	29,490
No. who developed a second primary cancer	584	705	1,289
Average age at diagnosis of first cancer, yr	67	67	67
Average yr of diagnosis of first cancer	1966	1966	1966
Person-yr of follow-up	45,525	64,001	109,526
Average follow-up, yr	3.5	3.9	3.8
Percent given radiotherapy for first cancer	4	4	4

[a] ICD-7 code = 153.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the colon or rectosigmoid junction in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	1,060	82.2
Only the first cancer	147	11.4
Only the second cancer	63	4.9
Neither first nor second cancer	19	1.5
Total second primary cancers	1,289	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

COLON
BOTH SEXES

TABLE 4C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the colon or rectosigmoid junction among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	29,490			16,825			6,741			3,399			29,490		
Person-yr in interval	22,204			40,549			23,982			22,792			109,526		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**172**	**256.27**	**0.7^b**	**466**	**484.15**	**1.0**	**311**	**307.62**	**1.0**	**340**	**321.94**	**1.1**	**1,289**	**1,369.98**	**0.9^b**
All excluding site of initial cancer	**160**	**230.22**	**0.7^b**	**431**	**434.11**	**1.0**	**284**	**274.54**	**1.0**	**304**	**285.02**	**1.1**	**1,179**	**1,223.90**	**1.0**
Buccal cavity, pharynx	**3**	**5.76**	**0.5**	**14**	**10.60**	**1.3**	**6**	**6.49**	**0.9**	**5**	**6.40**	**0.8**	**28**	**29.24**	**1.0**
Lip	1	2.47	0.4	7	4.49	1.6	3	2.66	1.1	2	2.44	0.8	13	12.06	1.1
Tongue	1	0.61	1.6	2	1.13	1.8	1	0.70	1.4	0	0.72	0.0	4	3.17	1.3
Salivary gland	0	0.67	0.0	1	1.23	0.8	0	0.76	0.0	0	0.71	0.0	1	3.37	0.3
Gum, other mouth	1	1.10	0.9	0	2.08	0.0	2	1.36	1.5	2	1.53	1.3	5	6.05	0.8
Pharynx	0	0.92	0.0	4	1.68	2.4	0	1.00	0.0	1	0.97	1.0	5	4.59	1.1
Digestive system	**62**	**96.45**	**0.6^b**	**151**	**180.22**	**0.8^b**	**93**	**115.70**	**0.8^b**	**137**	**121.30**	**1.1**	**443**	**513.66**	**0.9^b**
Esophagus	1	3.57	0.3	2	6.45	0.3	2	4.04	0.5	5	4.07	1.2	10	18.12	0.6
Stomach	14	27.83	0.5^b	34	49.86	0.7^b	26	31.14	0.8	23	30.12	0.8	97	138.93	0.7^b
Colon	12	26.05	0.5^b	35	50.04	0.7^b	27	33.08	0.8	36	36.92	1.0	110	146.08	0.8^b
Rectum	14	19.05	0.7	48	35.51	1.4	16	22.37	0.7	37	22.70	1.6^b	115	99.64	1.2
Liver, biliary	3	6.74	0.4	9	13.22	0.7	7	8.85	0.8	12	10.07	1.2	31	38.87	0.8
Pancreas	12	9.80	1.2	17	19.05	0.9	12	12.44	1.0	19	13.68	1.4	60	54.96	1.1
Respiratory system	**10**	**31.92**	**0.3^b**	**50**	**60.66**	**0.8**	**39**	**36.80**	**1.1**	**48**	**36.92**	**1.3**	**147**	**166.31**	**0.9**
Nasal cavities, sinuses	0	0.55	0.0	0	1.00	0.0	0	0.62	0.0	2	0.61	3.3	2	2.78	0.7
Larynx	1	1.95	0.5	6	3.66	1.6	2	2.18	0.9	5	2.10	2.4	14	9.89	1.4
Trachea, bronchus, lung	8	27.67	0.3^b	44	52.70	0.8	37	31.91	1.2	40	32.10	1.2	129	144.37	0.9
Female breast	13	24.79	0.5^b	40	47.35	0.8	41	31.11	1.3	37	35.49	1.0	131	138.74	0.9
Female genital tract	**35**	**21.28**	**1.6^b**	**99**	**40.25**	**2.5^b**	**44**	**25.44**	**1.7^b**	**27**	**27.21**	**1.0**	**205**	**114.19**	**1.8^b**
Cervix uteri	5	6.26	0.8	10	11.54	0.9	8	6.95	1.2	10	6.81	1.5	33	31.56	1.0
Corpus uteri	1	6.28	0.2^b	30	12.04	2.5^b	19	7.65	2.5^b	10	8.29	1.2	60	34.25	1.8^b
Uterus, NOS	2	0.55	3.7	3	0.98	3.1	1	0.65	1.5	0	0.71	0.0	6	2.88	2.1
Ovary, fallopian tubes	26	6.60	3.9^b	51	12.65	4.0^b	13	8.13	1.6	3	8.95	0.3^b	93	36.33	2.6^b
Prostate gland	17	19.46	0.9	25	37.42	0.7^b	28	23.72	1.2	23	22.87	1.0	93	103.47	0.9
Testis	0	0.40	0.0	0	0.72	0.0	0	0.40	0.0	0	0.34	0.0	0	1.86	0.0
Kidney, renal pelvis, ureter	7	7.54	0.9	11	14.42	0.8	6	9.18	0.7	6	9.69	0.6	30	40.82	0.7
Bladder, other urinary	9	14.34	0.6	20	27.54	0.7	21	17.37	1.2	14	18.00	0.8	64	77.25	0.8
Melanoma of the skin	1	2.55	0.4	7	4.89	1.4	2	3.11	0.6	4	3.37	1.2	14	13.91	1.0
Eye	0	0.71	0.0	2	1.31	1.5	0	0.82	0.0	2	0.81	2.5	4	3.65	1.1
Brain, central nervous system	3	3.99	0.8	8	7.51	1.1	6	4.54	1.3	4	4.56	0.9	21	20.61	1.0
Thyroid gland	0	1.23	0.0	1	2.35	0.4	4	1.53	2.6	2	1.71	1.2	7	6.82	1.0
Bone	0	0.43	0.0	0	0.79	0.0	1	0.48	2.1	1	0.47	2.1	2	2.17	0.9
Connective tissue	0	0.83	0.0	4	1.50	2.7	2	0.92	2.2	0	0.89	0.0	6	4.14	1.4
Lymphatic, hematopoietic system	**10**	**15.16**	**0.7**	**28**	**29.21**	**1.0**	**15**	**18.70**	**0.8**	**29**	**19.81**	**1.5**	**82**	**82.87**	**1.0**
Non-Hodgkin's lymphoma	2	4.16	0.5	10	8.00	1.3	4	5.14	0.8	9	5.53	1.6	25	22.83	1.1
Hodgkin's disease	0	0.97	0.0	1	1.84	0.5	1	1.12	0.9	1	1.12	0.9	3	5.05	0.6
Multiple myeloma	2	2.95	0.7	3	5.73	0.5	2	3.71	0.5	4	3.97	1.0	11	16.37	0.7
Leukemias	6	6.94	0.9	14	13.36	1.0	8	8.57	0.9	15	9.02	1.7	43	37.87	1.1
Chronic lymphocytic	0	3.62	0.0	5	6.94	0.7	4	4.48	0.9	5	4.69	1.1	14	19.73	0.7
Acute nonlymphocytic	4	1.76	2.3	6	3.48	1.7	1	2.25	0.4	0	2.50	0.0	11	10.00	1.1

[a] ICD-7 code = 153.

[b] $P < .05$.

COLON
MALES

TABLE 4D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the colon or rectosigmoid junction among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	13,093			7,478			2,843			1,338			13,093		
Person-yr in interval	9,852			17,627			9,847			8,199			45,525		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**80**	**132.30**	**0.6**[b]	**207**	**247.24**	**0.8**[b]	**137**	**150.00**	**0.9**	**160**	**139.69**	**1.1**	**584**	**669.23**	**0.9**[b]
All excluding site of initial cancer	**74**	**120.50**	**0.6**[b]	**191**	**225.03**	**0.8**[b]	**129**	**136.17**	**0.9**	**147**	**126.42**	**1.2**	**541**	**608.12**	**0.9**[b]
Buccal cavity, pharynx	**3**	**4.05**	**0.7**	**11**	**7.34**	**1.5**	**4**	**4.30**	**0.9**	**4**	**3.82**	**1.0**	**22**	**19.50**	**1.1**
Lip	1	2.20	0.5	5	3.98	1.3	3	2.32	1.3	2	2.04	1.0	11	10.54	1.0
Tongue	1	0.30	3.3	2	0.55	3.6	0	0.31	0.0	0	0.26	0.0	3	1.43	2.1
Salivary gland	0	0.33	0.0	0	0.60	0.0	0	0.36	0.0	0	0.31	0.0	0	1.60	0.0
Gum, other mouth	1	0.59	1.7	0	1.08	0.0	1	0.65	1.5	1	0.62	1.6	3	2.93	1.0
Pharynx	0	0.63	0.0	4	1.14	3.5	0	0.65	0.0	1	0.58	1.7	5	3.01	1.7
Digestive system	**36**	**50.82**	**0.7**[b]	**79**	**93.47**	**0.8**	**47**	**56.71**	**0.8**	**62**	**51.52**	**1.2**	**224**	**252.51**	**0.9**
Esophagus	0	2.25	0.0	1	3.99	0.3	2	2.34	0.9	3	2.04	1.5	6	10.61	0.6
Stomach	7	16.05	0.4[b]	22	28.71	0.8	14	17.12	0.8	13	14.65	0.9	56	76.52	0.7[b]
Colon	6	11.80	0.5	16	22.21	0.7	8	13.83	0.6	13	13.27	1.0	43	61.11	0.7[b]
Rectum	11	11.24	1.0	26	20.66	1.3	10	12.42	0.8	19	11.19	1.7[b]	66	55.51	1.2
Liver, biliary	2	2.77	0.7	4	5.31	0.8	4	3.32	1.2	3	3.23	0.9	13	14.62	0.9
Pancreas	7	5.16	1.4	7	9.82	0.7	7	6.04	1.2	10	5.72	1.7	31	26.74	1.2
Respiratory system	**6**	**25.49**	**0.2**[b]	**38**	**47.99**	**0.8**	**24**	**28.31**	**0.8**	**39**	**26.70**	**1.5**[b]	**107**	**128.49**	**0.8**
Nasal cavities, sinuses	0	0.36	0.0	0	0.65	0.0	0	0.39	0.0	1	0.35	2.9	1	1.75	0.6
Larynx	0	1.70	0.0	5	3.17	1.6	2	1.86	1.1	4	1.74	2.3	11	8.47	1.3
Trachea, bronchus, lung	6	22.24	0.3[b]	33	41.94	0.8	22	24.68	0.9	33	23.33	1.4	94	112.18	0.8
Prostate gland	17	19.46	0.9	25	37.42	0.7[b]	28	23.72	1.2	23	22.87	1.0	93	103.47	0.9
Testis	0	0.40	0.0	0	0.72	0.0	0	0.40	0.0	0	0.34	0.0	0	1.86	0.0
Kidney, renal pelvis, ureter	3	4.23	0.7	8	7.97	1.0	5	4.84	1.0	4	4.59	0.9	20	21.62	0.9
Bladder, other urinary	6	10.70	0.6	16	20.36	0.8	12	12.45	1.0	11	12.01	0.9	45	55.52	0.8
Melanoma of the skin	1	1.02	1.0	5	1.91	2.6	1	1.16	0.9	1	1.09	0.9	8	5.17	1.5
Eye	0	0.38	0.0	0	0.69	0.0	0	0.41	0.0	0	0.37	0.0	0	1.85	0.0
Brain, central nervous system	1	1.85	0.5	6	3.38	1.8	4	1.92	2.1	1	1.70	0.6	12	8.86	1.4
Thyroid gland	0	0.36	0.0	0	0.67	0.0	2	0.40	5.0	0	0.37	0.0	2	1.80	1.1
Bone	0	0.23	0.0	0	0.41	0.0	0	0.24	0.0	0	0.21	0.0	0	1.09	0.0
Connective tissue	0	0.44	0.0	3	0.78	3.8	2	0.46	4.3	0	0.40	0.0	5	2.08	2.4
Lymphatic, hematopoietic system	**6**	**8.45**	**0.7**	**13**	**16.01**	**0.8**	**7**	**9.74**	**0.7**	**15**	**9.09**	**1.7**	**41**	**43.28**	**0.9**
Non-Hodgkin's lymphoma	2	2.15	0.9	6	4.05	1.5	2	2.45	0.8	5	2.28	2.2	15	10.93	1.4
Hodgkin's disease	0	0.54	0.0	0	1.00	0.0	0	0.58	0.0	0	0.52	0.0	0	2.64	0.0
Multiple myeloma	1	1.59	0.6	2	3.03	0.7	2	1.86	1.1	2	1.74	1.1	7	8.22	0.9
Leukemias	3	4.09	0.7	5	7.77	0.6	3	4.76	0.6	8	4.46	1.8	19	21.07	0.9
Chronic lymphocytic	0	2.32	0.0	2	4.39	0.5	2	2.71	0.7	1	2.53	0.4	5	11.95	0.4[b]
Acute nonlymphocytic	2	0.95	2.1	2	1.85	1.1	0	1.14	0.0	0	1.12	0.0	4	5.06	0.8

[a] ICD-7 code = 153.

[b] $P < .05$.

COLON FEMALES

TABLE 4E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the colon or rectosigmoid junction among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	16,397			9,347			3,898			2,061			16,397		
Person-yr in interval	12,352			22,922			14,135			14,592			64,001		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**92**	**123.97**	**0.7**[b]	**259**	**236.91**	**1.1**	**174**	**157.62**	**1.1**	**180**	**182.25**	**1.0**	**705**	**700.75**	**1.0**
All excluding site of initial cancer	**86**	**109.72**	**0.8**[b]	**240**	**209.08**	**1.1**[b]	**155**	**138.37**	**1.1**	**157**	**158.60**	**1.0**	**638**	**615.78**	**1.0**
Buccal cavity, pharynx	**0**	**1.71**	**0.0**	**3**	**3.26**	**0.9**	**2**	**2.19**	**0.9**	**1**	**2.58**	**0.4**	**6**	**9.74**	**0.6**
Lip	0	0.27	0.0	2	0.51	3.9	0	0.34	0.0	0	0.40	0.0	2	1.52	1.3
Tongue	0	0.31	0.0	0	0.58	0.0	1	0.39	2.6	0	0.46	0.0	1	1.74	0.6
Salivary gland	0	0.34	0.0	1	0.63	1.6	0	0.40	0.0	0	0.40	0.0	1	1.77	0.6
Gum, other mouth	0	0.51	0.0	0	1.00	0.0	1	0.71	1.4	1	0.91	1.1	2	3.12	0.6
Pharynx	0	0.29	0.0	0	0.54	0.0	0	0.35	0.0	0	0.39	0.0	0	1.58	0.0
Digestive system	**26**	**45.63**	**0.6**[b]	**72**	**86.75**	**0.8**	**46**	**58.99**	**0.8**	**75**	**69.78**	**1.1**	**219**	**261.15**	**0.8**[b]
Esophagus	1	1.32	0.8	1	2.46	0.4	0	1.70	0.0	2	2.03	1.0	4	7.51	0.5
Stomach	7	11.78	0.6	12	21.15	0.6[b]	12	14.02	0.9	10	15.47	0.6	41	62.41	0.7[b]
Colon	6	14.25	0.4[b]	19	27.83	0.7	19	19.25	1.0	23	23.65	1.0	67	84.97	0.8
Rectum	3	7.81	0.4	22	14.85	1.5	6	9.95	0.6	18	11.51	1.6	49	44.13	1.1
Liver, biliary	1	3.97	0.3	5	7.91	0.6	3	5.53	0.5	9	6.84	1.3	18	24.25	0.7
Pancreas	5	4.64	1.1	10	9.23	1.1	5	6.40	0.8	9	7.96	1.1	29	28.22	1.0
Respiratory system	**4**	**6.43**	**0.6**	**12**	**12.67**	**0.9**	**15**	**8.49**	**1.8**	**9**	**10.22**	**0.9**	**40**	**37.82**	**1.1**
Nasal cavities, sinuses	0	0.19	0.0	0	0.35	0.0	0	0.23	0.0	1	0.26	3.9	1	1.03	1.0
Larynx	1	0.25	3.9	1	0.49	2.0	0	0.32	0.0	1	0.36	2.8	3	1.42	2.1
Trachea, bronchus, lung	2	5.43	0.4	11	10.76	1.0	15	7.23	2.1[b]	7	8.77	0.8	35	32.19	1.1
Female breast	13	24.79	0.5[b]	40	47.35	0.8	41	31.11	1.3	37	35.49	1.0	131	138.74	0.9
Female genital tract	**35**	**21.28**	**1.6**[b]	**99**	**40.25**	**2.5**[b]	**44**	**25.44**	**1.7**[b]	**27**	**27.21**	**1.0**	**205**	**114.19**	**1.8**[b]
Cervix uteri	5	6.26	0.8	10	11.54	0.9	8	6.95	1.2	10	6.81	1.5	33	31.56	1.0
Corpus uteri	1	6.28	0.2[b]	30	12.04	2.5[b]	19	7.65	2.5[b]	10	8.29	1.2	60	34.25	1.8[b]
Uterus, NOS	2	0.55	3.7	3	0.98	3.1	1	0.65	1.5	0	0.71	0.0	6	2.88	2.1
Ovary, fallopian tubes	26	6.60	3.9[b]	51	12.65	4.0[b]	13	8.13	1.6	3	8.95	0.3[b]	93	36.33	2.6[b]
Kidney, renal pelvis, ureter	4	3.31	1.2	3	6.45	0.5	1	4.34	0.2	2	5.10	0.4	10	19.20	0.5[b]
Bladder, other urinary	3	3.64	0.8	4	7.18	0.6	9	4.92	1.8	3	5.99	0.5	19	21.73	0.9
Melanoma of the skin	0	1.53	0.0	2	2.98	0.7	1	1.95	0.5	3	2.28	1.3	6	8.74	0.7
Eye	0	0.33	0.0	2	0.62	3.2	0	0.41	0.0	2	0.44	4.5	4	1.80	2.2
Brain, central nervous system	2	2.14	0.9	2	4.13	0.5	2	2.62	0.8	3	2.86	1.1	9	11.75	0.8
Thyroid gland	0	0.87	0.0	1	1.68	0.6	2	1.13	1.8	2	1.34	1.5	5	5.02	1.0
Bone	0	0.20	0.0	0	0.38	0.0	1	0.24	4.1	1	0.26	3.8	2	1.08	1.8
Connective tissue	0	0.39	0.0	1	0.72	1.4	0	0.46	0.0	0	0.49	0.0	1	2.06	0.5
Lymphatic, hematopoietic system	**4**	**6.71**	**0.6**	**15**	**13.20**	**1.1**	**8**	**8.96**	**0.9**	**14**	**10.72**	**1.3**	**41**	**39.59**	**1.0**
Non-Hodgkin's lymphoma	0	2.01	0.0	4	3.95	1.0	2	2.69	0.7	4	3.25	1.2	10	11.90	0.8
Hodgkin's disease	0	0.43	0.0	1	0.84	1.2	1	0.54	1.8	1	0.60	1.7	3	2.41	1.2
Multiple myeloma	1	1.36	0.7	1	2.70	0.4	0	1.85	0.0	2	2.23	0.9	4	8.15	0.5
Leukemias	3	2.85	1.1	9	5.59	1.6	5	3.81	1.3	7	4.56	1.5	24	16.80	1.4
Chronic lymphocytic	0	1.30	0.0	3	2.55	1.2	2	1.77	1.1	4	2.16	1.8	9	7.78	1.2
Acute nonlymphocytic	2	0.81	2.5	4	1.63	2.5	1	1.11	0.9	0	1.38	0.0	7	4.94	1.4

[a] ICD-7 code = 153.

[b] $P < .05$.

RECTUM
BOTH SEXES

TABLE 5A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the rectum (excluding rectosigmoid junction and anus), 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	15,442	11,155	26,597
No. who developed a second primary cancer	581	387	968
Average age at diagnosis of first cancer, yr	67	66	67
Average yr of diagnosis of first cancer	1964	1964	1964
Person-yr of follow-up	58,436	48,759	107,195
Average follow-up, yr	3.8	4.4	4.1
Percent given radiotherapy for first cancer	11	11	11

[a] ICD-7 code = 154.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 5B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the rectum (excluding rectosigmoid junction and anus) in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	811	83.8
Only the first cancer	106	11.0
Only the second cancer	30	3.1
Neither first nor second cancer	21	2.2
Total second primary cancers	968	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

RECTUM
BOTH SEXES

TABLE 5C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the rectum (excluding rectosigmoid junction and anus) among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	26,597			17,057			6,299			3,263			26,597		
Person-yr in interval	21,404			39,660			22,534			23,597			107,195		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**105**	**244.19**	**0.4^b**	**339**	**466.21**	**0.7^b**	**242**	**289.98**	**0.8^b**	**282**	**362.20**	**0.8^b**	**968**	**1,362.59**	**0.7^b**
All excluding site of initial cancer	**105**	**224.67**	**0.5^b**	**339**	**430.01**	**0.8^b**	**242**	**267.96**	**0.9**	**282**	**335.46**	**0.8^b**	**968**	**1,258.11**	**0.8^b**
Buccal cavity, pharynx	**1**	**6.27**	**0.2^b**	**11**	**11.54**	**1.0**	**9**	**6.76**	**1.3**	**5**	**7.79**	**0.6**	**26**	**32.37**	**0.8**
Lip	0	2.97	0.0	3	5.43	0.6	4	3.08	1.3	3	3.38	0.9	10	14.86	0.7
Tongue	0	0.61	0.0	0	1.10	0.0	1	0.66	1.5	0	0.77	0.0	1	3.15	0.3
Salivary gland	0	0.66	0.0	1	1.24	0.8	0	0.75	0.0	0	0.83	0.0	1	3.48	0.3
Gum, other mouth	0	1.04	0.0	4	1.94	2.1	0	1.22	0.0	1	1.64	0.6	5	5.85	0.9
Pharynx	1	1.00	1.0	3	1.82	1.6	4	1.04	3.8^b	1	1.17	0.9	9	5.03	1.8
Digestive system	**24**	**94.92**	**0.3^b**	**80**	**175.82**	**0.5^b**	**76**	**108.79**	**0.7^b**	**98**	**136.56**	**0.7^b**	**278**	**516.10**	**0.5^b**
Esophagus	1	3.88	0.3	5	6.81	0.7	3	3.99	0.8	3	4.77	0.6	12	19.45	0.6
Stomach	9	29.90	0.3^b	22	52.56	0.4^b	12	30.93	0.4^b	33	35.57	0.9	76	148.95	0.5^b
Colon	5	23.48	0.2^b	35	45.04	0.8	45	29.17	1.5^b	47	39.54	1.2	132	137.22	1.0
Rectum	0	19.52	0.0^b	0	36.20	0.0^b	0	22.02	0.0^b	0	26.74	0.0^b	0	104.48	0.0^b
Liver, biliary	6	5.74	1.0	6	11.45	0.5	8	7.64	1.0	4	10.58	0.4^b	24	35.42	0.7
Pancreas	3	9.01	0.3^b	8	17.80	0.4^b	7	11.54	0.6	8	15.30	0.5	26	53.65	0.5^b
Respiratory system	**15**	**33.50**	**0.4^b**	**54**	**66.46**	**0.8**	**43**	**40.25**	**1.1**	**36**	**47.97**	**0.8**	**148**	**188.19**	**0.8^b**
Nasal cavities, sinuses	1	0.57	1.8	0	1.06	0.0	0	0.64	0.0	0	0.73	0.0	1	3.01	0.3
Larynx	3	2.17	1.4	4	4.20	1.0	3	2.46	1.2	4	2.79	1.4	14	11.62	1.2
Trachea, bronchus, lung	11	28.94	0.4^b	45	57.72	0.8	39	34.98	1.1	32	41.81	0.8	127	163.45	0.8^b
Female breast	12	17.30	0.7	38	33.66	1.1	26	22.29	1.2	27	29.56	0.9	103	102.80	1.0
Female genital tract	**11**	**15.23**	**0.7**	**29**	**29.84**	**1.0**	**16**	**19.06**	**0.8**	**27**	**23.13**	**1.2**	**83**	**87.26**	**1.0**
Cervix uteri	1	4.68	0.2	6	8.97	0.7	1	5.37	0.2	10	5.73	1.7	18	24.74	0.7
Corpus uteri	3	4.42	0.7	7	8.86	0.8	8	5.75	1.4	10	7.12	1.4	28	26.15	1.1
Uterus, NOS	0	0.41	0.0	0	0.71	0.0	0	0.46	0.0	0	0.59	0.0	0	2.18	0.0
Ovary, fallopian tubes	7	4.63	1.5	13	9.20	1.4	5	6.04	0.8	5	7.65	0.7	30	27.51	1.1
Prostate gland	9	22.37	0.4^b	45	43.37	1.0	31	27.14	1.1	22	34.85	0.6^b	7	127.72	0.8^b
Testis	0	0.46	0.0	1	0.83	1.2	0	0.44	0.0	3	0.43	7.0^b	4	2.17	1.8
Kidney, renal pelvis, ureter	9	7.20	1.3	16	14.03	1.1	9	8.83	1.0	9	11.12	0.8	43	41.17	1.0
Bladder, other urinary	12	14.59	0.8	27	28.76	0.9	13	17.96	0.7	18	22.78	0.8	70	84.09	0.8
Melanoma of the skin	1	2.19	0.5	5	4.29	1.2	3	2.70	1.1	2	3.39	0.6	11	12.57	0.9
Eye	1	0.71	1.4	2	1.34	1.5	0	0.80	0.0	0	0.93	0.0	3	3.78	0.8
Brain, central nervous system	1	3.74	0.3	3	7.29	0.4	3	4.32	0.7	4	4.83	0.8	11	20.17	0.5^b
Thyroid gland	2	1.02	2.0	0	1.99	0.0	0	1.30	0.0	1	1.67	0.6	3	5.99	0.5
Bone	0	0.44	0.0	0	0.81	0.0	1	0.48	2.1	0	0.55	0.0	1	2.28	0.4
Connective tissue	0	0.84	0.0	2	1.54	1.3	1	0.89	1.1	2	1.01	2.0	5	4.28	1.2
Lymphatic, hematopoietic system	**6**	**14.42**	**0.4^b**	**24**	**28.22**	**0.9**	**9**	**17.88**	**0.5^b**	**21**	**22.67**	**0.9**	**60**	**83.18**	**0.7^b**
Non-Hodgkin's lymphoma	4	3.84	1.0	7	7.53	0.9	1	4.78	0.2	5	6.10	0.8	17	22.25	0.8
Hodgkin's disease	1	0.96	1.0	3	1.85	1.6	0	1.11	0.0	0	1.26	0.0	4	5.19	0.8
Multiple myeloma	0	2.75	0.0	1	5.46	0.2	2	3.52	0.6	3	4.53	0.7	6	16.25	0.4^b
Leukemias	1	6.73	0.1^b	13	13.12	1.0	6	8.29	0.7	13	10.59	1.2	33	38.72	0.9
Chronic lymphocytic	0	3.63	0.0	8	7.03	1.1	5	4.43	1.1	8	5.69	1.4	21	20.76	1.0
Acute nonlymphocytic	1	1.55	0.6	3	3.16	0.9	1	2.07	0.5	4	2.81	1.4	9	9.59	0.9

[a] ICD-7 code = 154.

[b] $P < .05$.

RECTUM
MALES

TABLE 5D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the rectum (excluding rectosigmoid junction and anus) among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	15,442			9,891			3,471			1,681			15,442		
Person-yr in interval	12,435			22,552			12,000			11,450			58,436		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**61**	**158.07**	**0.4^b**	**203**	**299.62**	**0.7^b**	**159**	**177.77**	**0.9**	**158**	**209.82**	**0.8^b**	**581**	**845.29**	**0.7^b**
All excluding site of initial cancer	**61**	**144.03**	**0.4^b**	**203**	**273.88**	**0.7^b**	**159**	**162.82**	**1.0**	**158**	**192.77**	**0.8^b**	**581**	**773.50**	**0.8^b**
Buccal cavity, pharynx	**0**	**5.08**	**0.0^b**	**6**	**9.27**	**0.6**	**9**	**5.22**	**1.7**	**4**	**5.66**	**0.7**	**19**	**25.23**	**0.8**
Lip	0	2.79	0.0	2	5.08	0.4	4	2.84	1.4	3	3.04	1.0	9	13.75	0.7
Tongue	0	0.39	0.0	0	0.70	0.0	1	0.39	2.6	0	0.39	0.0	1	1.87	0.5
Salivary gland	0	0.41	0.0	0	0.76	0.0	0	0.44	0.0	0	0.48	0.0	0	2.09	0.0
Gum, other mouth	0	0.71	0.0	2	1.30	1.5	0	0.76	0.0	0	0.90	0.0	2	3.67	0.5
Pharynx	0	0.79	0.0	2	1.43	1.4	4	0.79	5.0^b	1	0.84	1.2	7	3.85	1.8
Digestive system	**16**	**63.22**	**0.3^b**	**51**	**115.84**	**0.4^b**	**50**	**67.59**	**0.7^b**	**59**	**78.42**	**0.8^b**	**176**	**325.08**	**0.5^b**
Esophagus	1	2.95	0.3	5	5.12	1.0	2	2.83	0.7	2	3.09	0.6	10	13.99	0.7
Stomach	6	21.16	0.3^b	15	37.18	0.4^b	9	20.91	0.4^b	24	22.65	1.1	54	101.90	0.5^b
Colon	4	13.95	0.3^b	21	26.37	0.8	27	15.96	1.7^b	27	19.95	1.4	79	76.22	1.0
Rectum	0	14.04	0.0^b	0	25.74	0.0^b	0	14.95	0.0^b	0	17.05	0.0^b	0	71.79	0.0^b
Liver, biliary	2	3.14	0.6	3	6.20	0.5	7	3.83	1.8	2	4.86	0.4	14	18.04	0.8
Pancreas	3	5.98	0.5	4	11.70	0.3^b	4	7.15	0.6	4	8.68	0.5	15	33.51	0.4^b
Respiratory system	**14**	**29.26**	**0.5^b**	**45**	**57.90**	**0.8**	**35**	**34.29**	**1.0**	**31**	**39.46**	**0.8**	**125**	**160.92**	**0.8^b**
Nasal cavities, sinuses	1	0.44	2.3	0	0.81	0.0	0	0.47	0.0	0	0.51	0.0	1	2.23	0.4
Larynx	3	2.00	1.5	3	3.86	0.8	2	2.23	0.9	3	2.49	1.2	11	10.58	1.0
Trachea, bronchus, lung	10	25.40	0.4^b	39	50.51	0.8	32	29.94	1.1	28	34.51	0.8	109	140.36	0.8^b
Prostate gland	9	22.37	0.4^b	45	43.37	1.0	31	27.14	1.1	22	34.85	0.6^b	107	127.72	0.8
Testis	0	0.46	0.0	1	0.83	1.2	0	0.44	0.0	3	0.43	7.0^b	4	2.17	1.8
Kidney, renal pelvis, ureter	7	4.96	1.4	12	9.56	1.3	7	5.74	1.2	7	6.82	1.0	33	27.08	1.2
Bladder, other urinary	7	12.19	0.6	23	23.94	1.0	11	14.54	0.8	12	17.77	0.7	53	68.44	0.8
Melanoma of the skin	1	1.18	0.8	1	2.25	0.4	3	1.32	2.3	0	1.52	0.0	5	6.27	0.8
Eye	0	0.47	0.0	0	0.88	0.0	0	0.50	0.0	0	0.55	0.0	0	2.40	0.0
Brain, central nervous system	0	2.24	0.0	2	4.29	0.5	3	2.36	1.3	2	2.38	0.8	7	11.27	0.6
Thyroid gland	2	0.43	4.6	0	0.83	0.0	0	0.49	0.0	1	0.55	1.8	3	2.31	1.3
Bone	0	0.29	0.0	0	0.53	0.0	1	0.30	3.3	0	0.32	0.0	1	1.45	0.7
Connective tissue	0	0.56	0.0	1	1.01	1.0	1	0.55	1.8	2	0.59	3.4	4	2.71	1.5
Lymphatic, hematopoietic system	**5**	**9.92**	**0.5**	**15**	**19.21**	**0.8**	**6**	**11.56**	**0.5**	**11**	**13.67**	**0.8**	**37**	**54.36**	**0.7^b**
Non-Hodgkin's lymphoma	3	2.51	1.2	5	4.86	1.0	0	2.90	0.0	2	3.38	0.6	10	13.65	0.7
Hodgkin's disease	1	0.66	1.5	2	1.24	1.6	0	0.71	0.0	0	0.75	0.0	3	3.37	0.9
Multiple myeloma	0	1.84	0.0	0	3.62	0.0	1	2.21	0.5	1	2.65	0.4	2	10.33	0.2^b
Leukemias	1	4.81	0.2	8	9.30	0.9	5	5.62	0.9	8	6.76	1.2	22	26.48	0.8
Chronic lymphocytic	0	2.75	0.0	5	5.30	0.9	5	3.21	1.6	6	3.88	1.5	16	15.13	1.1
Acute nonlymphocytic	1	1.04	1.0	2	2.09	1.0	0	1.30	0.0	1	1.65	0.6	4	6.08	0.7

[a] ICD-7 code = 154.

[b] $P < .05$.

RECTUM
FEMALES

TABLE 5E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the rectum (excluding rectosigmoid junction and anus) among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	11,155			7,166			2,828			1,582			11,155		
Person-yr in interval	8,969			17,108			10,534			12,147			48,759		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**44**	**86.12**	**0.5**[b]	**136**	**166.59**	**0.8**[b]	**83**	**112.21**	**0.7**[b]	**124**	**152.38**	**0.8**[b]	**387**	**517.30**	**0.7**[b]
All excluding site of initial cancer	**44**	**80.64**	**0.5**[b]	**136**	**156.13**	**0.9**	**83**	**105.14**	**0.8**[b]	**124**	**142.69**	**0.9**	**387**	**484.61**	**0.8**[b]
Buccal cavity, pharynx	**1**	**1.19**	**0.8**	**5**	**2.27**	**2.2**	**0**	**1.54**	**0.0**	**1**	**2.13**	**0.5**	**7**	**7.14**	**1.0**
Lip	0	0.18	0.0	1	0.35	2.9	0	0.24	0.0	0	0.34	0.0	1	1.11	0.9
Tongue	0	0.22	0.0	0	0.40	0.0	0	0.27	0.0	0	0.38	0.0	0	1.28	0.0
Salivary gland	0	0.25	0.0	1	0.48	2.1	0	0.31	0.0	0	0.35	0.0	1	1.39	0.7
Gum, other mouth	0	0.33	0.0	2	0.64	3.1	0	0.46	0.0	1	0.74	1.4	3	2.18	1.4
Pharynx	1	0.21	4.8	1	0.39	2.5	0	0.25	0.0	0	0.33	0.0	2	1.18	1.7
Digestive system	**8**	**31.70**	**0.3**[b]	**29**	**59.98**	**0.5**[b]	**26**	**41.20**	**0.6**[b]	**39**	**58.14**	**0.7**[b]	**102**	**191.02**	**0.5**[b]
Esophagus	0	0.93	0.0	0	1.69	0.0	1	1.16	0.9	1	1.68	0.6	2	5.46	0.4
Stomach	3	8.74	0.3	7	15.38	0.5[b]	3	10.02	0.3[b]	9	12.92	0.7	22	47.05	0.5[b]
Colon	1	9.53	0.1[b]	14	18.67	0.7	18	13.21	1.4	20	19.59	1.0	53	61.00	0.9
Rectum	0	5.48	0.0[b]	0	10.46	0.0[b]	0	7.07	0.0[b]	0	9.69	0.0[b]	0	32.69	0.0[b]
Liver, biliary	4	2.60	1.5	3	5.25	0.6	1	3.81	0.3	2	5.72	0.3	10	17.38	0.6
Pancreas	0	3.03	0.0	4	6.10	0.7	3	4.39	0.7	4	6.62	0.6	11	20.14	0.5[b]
Respiratory system	**1**	**4.24**	**0.2**	**9**	**8.56**	**1.1**	**8**	**5.96**	**1.3**	**5**	**8.51**	**0.6**	**23**	**27.27**	**0.8**
Nasal cavities, sinuses	0	0.13	0.0	0	0.25	0.0	0	0.17	0.0	0	0.22	0.0	0	0.78	0.0
Larynx	0	0.17	0.0	1	0.34	2.9	1	0.23	4.4	1	0.30	3.3	3	1.04	2.9
Trachea, bronchus, lung	1	3.54	0.3	6	7.21	0.8	7	5.04	1.4	4	7.30	0.5	18	23.09	0.8
Female breast	12	17.30	0.7	38	33.66	1.1	26	22.29	1.2	27	29.56	0.9	103	102.80	1.0
Female genital tract	**11**	**15.23**	**0.7**	**29**	**29.84**	**1.0**	**16**	**19.06**	**0.8**	**27**	**23.13**	**1.2**	**83**	**87.26**	**1.0**
Cervix uteri	1	4.68	0.2	6	8.97	0.7	1	5.37	0.2	10	5.73	1.7	18	24.74	0.7
Corpus uteri	3	4.42	0.7	7	8.86	0.8	8	5.75	1.4	10	7.12	1.4	28	26.15	1.1
Uterus, NOS	0	0.41	0.0	0	0.71	0.0	0	0.46	0.0	0	0.59	0.0	0	2.18	0.0
Ovary, fallopian tubes	7	4.63	1.5	13	9.20	1.4	5	6.04	0.8	5	7.65	0.7	30	27.51	1.1
Kidney, renal pelvis, ureter	2	2.24	0.9	4	4.47	0.9	2	3.09	0.6	2	4.30	0.5	10	14.09	0.7
Bladder, other urinary	5	2.40	2.1	4	4.82	0.8	2	3.42	0.6	6	5.01	1.2	17	15.65	1.1
Melanoma of the skin	0	1.01	0.0	4	2.04	2.0	0	1.38	0.0	2	1.87	1.1	6	6.30	1.0
Eye	1	0.24	4.3	2	0.46	4.3	0	0.30	0.0	0	0.38	0.0	3	1.38	2.2
Brain, central nervous system	1	1.50	0.7	1	3.00	0.3	0	1.96	0.0	2	2.45	0.8	4	8.90	0.4
Thyroid gland	0	0.59	0.0	0	1.16	0.0	0	0.81	0.0	0	1.12	0.0	0	3.68	0.0[b]
Bone	0	0.15	0.0	0	0.28	0.0	0	0.18	0.0	0	0.23	0.0	0	0.83	0.0
Connective tissue	0	0.28	0.0	1	0.53	1.9	0	0.34	0.0	0	0.42	0.0	1	1.57	0.6
Lymphatic, hematopoietic system	**1**	**4.50**	**0.2**	**9**	**9.01**	**1.0**	**3**	**6.32**	**0.5**	**10**	**9.00**	**1.1**	**23**	**28.82**	**0.8**
Non-Hodgkin's lymphoma	1	1.33	0.8	2	2.67	0.8	1	1.88	0.5	3	2.72	1.1	7	8.60	0.8
Hodgkin's disease	0	0.30	0.0	1	0.61	1.7	0	0.40	0.0	0	0.51	0.0	1	1.82	0.5
Multiple myeloma	0	0.91	0.0	1	1.84	0.5	1	1.31	0.8	2	1.88	1.1	4	5.92	0.7
Leukemias	0	1.92	0.0	5	3.82	1.3	1	2.67	0.4	5	3.83	1.3	11	12.24	0.9
Chronic lymphocytic	0	0.88	0.0	3	1.73	1.7	0	1.22	0.0	2	1.81	1.1	5	5.63	0.9
Acute nonlymphocytic	0	0.51	0.0	1	1.07	0.9	1	0.77	1.3	3	1.16	2.6	5	3.51	1.4

[a] ICD-7 code = 154.

[b] $P < .05$.

LIVER,
BILIARY
BOTH SEXES

TABLE 6A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the liver, gallbladder, or other biliary, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,642	2,811	4,453
No. who developed a second primary cancer	16	29	45
Average age at diagnosis of first cancer, yr	65	68	67
Average yr of diagnosis of first cancer	1967	1966	1966
Person-yr of follow-up	1,536	2,760	4,296
Average follow-up, yr	1.0	1.0	1.0
Percent given radiotherapy for first cancer	3	4	4

[a] ICD-7 code = 155.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 6B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the liver, gallbladder, or other biliary in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	36	80.0
Only the first cancer	4	8.9
Only the second cancer	5	11.1
Neither first nor second cancer	0	0.0
Total second primary cancers	45	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LIVER,
BILIARY
BOTH SEXES

TABLE 6C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the liver, gallbladder, or other biliary among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval		4,453			864			153			74			4,453	
Person-yr in interval		2,087			1,268			510			432			4,297	
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**17**	**23.04**	**0.7**	**16**	**14.76**	**1.1**	**6**	**6.12**	**1.0**	**6**	**6.00**	**1.0**	**45**	**49.92**	**0.9**
All excluding site of initial cancer	**17**	**22.40**	**0.8**	**14**	**14.33**	**1.0**	**5**	**5.92**	**0.8**	**6**	**5.80**	**1.0**	**42**	**48.44**	**0.9**
Buccal cavity, pharynx	**1**	**0.47**	**2.1**	**0**	**0.30**	**0.0**	**1**	**0.12**	**8.3**	**0**	**0.12**	**0.0**	**2**	**1.01**	**2.0**
Lip	0	0.19	0.0	0	0.12	0.0	1	0.04	25.0	0	0.04	0.0	1	0.39	2.6
Tongue	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.12	0.0
Salivary gland	1	0.06	16.7	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	1	0.13	7.7
Gum, other mouth	0	0.09	0.0	0	0.07	0.0	0	0.03	0.0	0	0.03	0.0	0	0.22	0.0
Pharynx	0	0.08	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.16	0.0
Digestive system	**4**	**8.47**	**0.5**	**8**	**5.42**	**1.5**	**2**	**2.31**	**0.9**	**1**	**2.30**	**0.4**	**15**	**18.51**	**0.8**
Esophagus	0	0.29	0.0	0	0.18	0.0	0	0.08	0.0	0	0.07	0.0	0	0.63	0.0
Stomach	0	2.35	0.0	1	1.42	0.7	0	0.58	0.0	0	0.57	0.0	1	4.92	0.2
Colon	2	2.36	0.8	3	1.57	1.9	1	0.70	1.4	1	0.71	1.4	7	5.33	1.3
Rectum	0	1.64	0.0	0	1.03	0.0	0	0.42	0.0	0	0.42	0.0	0	3.52	0.0
Liver, biliary	0	0.64	0.0	2	0.43	4.7	1	0.20	5.0	0	0.20	0.0	3	1.48	2.0
Pancreas	2	0.89	2.2	2	0.59	3.4	0	0.26	0.0	0	0.26	0.0	4	1.99	2.0
Respiratory system	**2**	**2.72**	**0.7**	**0**	**1.78**	**0.0**	**1**	**0.65**	**1.5**	**2**	**0.61**	**3.3**	**5**	**5.75**	**0.9**
Nasal cavities, sinuses	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.10	0.0
Larynx	0	0.16	0.0	0	0.11	0.0	0	0.04	0.0	1	0.03	33.3	1	0.33	3.0
Trachea, bronchus, lung	2	2.37	0.8	0	1.55	0.0	1	0.56	1.8	1	0.53	1.9	4	4.99	0.8
Female breast	2	2.67	0.7	1	1.71	0.6	0	0.82	0.0	0	0.75	0.0	3	5.95	0.5
Female genital tract	**3**	**2.30**	**1.3**	**5**	**1.42**	**3.5**[b]	**1**	**0.64**	**1.6**	**1**	**0.58**	**1.7**	**10**	**4.94**	**2.0**
Cervix uteri	0	0.65	0.0	0	0.39	0.0	0	0.16	0.0	1	0.15	6.9	1	1.34	0.7
Corpus uteri	0	0.70	0.0	3	0.43	7.0[b]	0	0.19	0.0	0	0.17	0.0	3	1.49	2.0
Uterus, NOS	0	0.06	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Ovary, fallopian tubes	3	0.73	4.1	1	0.46	2.2	1	0.21	4.8	0	0.19	0.0	5	1.58	3.2[b]
Prostate gland	0	1.33	0.0	1	0.86	1.2	0	0.26	0.0	1	0.35	2.9	2	2.80	0.7
Testis	0	0.03	0.0	1	0.02	53.9	0	0.01	0.0	0	0.00	0.0	1	0.06	16.7
Kidney, renal pelvis, ureter	2	0.69	2.9	0	0.44	0.0	0	0.18	0.0	0	0.18	0.0	2	1.49	1.3
Bladder, other urinary	1	1.20	0.8	0	0.80	0.0	1	0.31	3.2	0	0.31	0.0	2	2.61	0.8
Melanoma of the skin	0	0.24	0.0	0	0.16	0.0	0	0.07	0.0	0	0.06	0.0	0	0.52	0.0
Eye	0	0.07	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.14	0.0
Brain, central nervous system	0	0.38	0.0	0	0.25	0.0	0	0.09	0.0	1	0.09	11.1	1	0.81	1.2
Thyroid gland	1	0.12	8.3	0	0.08	0.0	0	0.04	0.0	0	0.04	0.0	1	0.28	3.6
Bone	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Connective tissue	1	0.07	14.3	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	1	0.15	6.7
Lymphatic, hematopoietic system	**0**	**1.37**	**0.0**	**0**	**0.89**	**0.0**	**0**	**0.37**	**0.0**	**0**	**0.37**	**0.0**	**0**	**3.00**	**0.0**
Non-Hodgkin's lymphoma	0	0.38	0.0	0	0.25	0.0	0	0.10	0.0	0	0.10	0.0	0	0.84	0.0
Hodgkin's disease	0	0.09	0.0	0	0.06	0.0	0	0.02	0.0	0	0.02	0.0	0	0.20	0.0
Multiple myeloma	0	0.27	0.0	0	0.18	0.0	0	0.07	0.0	0	0.08	0.0	0	0.59	0.0
Leukemias	0	0.61	0.0	0	0.40	0.0	0	0.17	0.0	0	0.17	0.0	0	1.34	0.0
Chronic lymphocytic	0	0.31	0.0	0	0.20	0.0	0	0.08	0.0	0	0.09	0.0	0	0.68	0.0
Acute nonlymphocytic	0	0.16	0.0	0	0.11	0.0	0	0.04	0.0	0	0.05	0.0	0	0.36	0.0

[a] ICD-7 code = 155.

[b] $P < .05$.

LIVER, BILIARY MALES

TABLE 6D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the liver, gallbladder, or other biliary among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,642			345			48			24			1,642		
Person-yr in interval	782			472			159			123			1,536		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**5**	**9.60**	**0.5**	**4**	**6.08**	**0.7**	**2**	**1.89**	**1.1**	**5**	**2.09**	**2.4**	**16**	**19.66**	**0.8**
All excluding site of initial cancer	**5**	**9.40**	**0.5**	**4**	**5.95**	**0.7**	**2**	**1.85**	**1.1**	**5**	**2.04**	**2.5**	**16**	**19.23**	**0.8**
Buccal cavity, pharynx	**1**	**0.29**	**3.4**	**0**	**0.18**	**0.0**	**1**	**0.06**	**17.4**	**0**	**0.06**	**0.0**	**2**	**0.59**	**3.4**
Lip	0	0.16	0.0	0	0.10	0.0	1	0.03	32.8	0	0.03	0.0	1	0.32	3.2
Tongue	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.04	0.0
Salivary gland	1	0.02	41.1	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	1	0.05	20.7
Gum, other mouth	0	0.04	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Pharynx	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Digestive system	**0**	**3.52**	**0.0**	**2**	**2.17**	**0.9**	**0**	**0.66**	**0.0**	**1**	**0.77**	**1.3**	**3**	**7.13**	**0.4**
Esophagus	0	0.15	0.0	0	0.09	0.0	0	0.03	0.0	0	0.03	0.0	0	0.30	0.0
Stomach	0	1.07	0.0	0	0.62	0.0	0	0.19	0.0	0	0.22	0.0	0	2.10	0.0
Colon	0	0.82	0.0	1	0.53	1.9	0	0.16	0.0	1	0.20	4.9	2	1.71	1.2
Rectum	0	0.79	0.0	0	0.48	0.0	0	0.15	0.0	0	0.17	0.0	0	1.59	0.0
Liver, biliary	0	0.20	0.0	0	0.13	0.0	0	0.04	0.0	0	0.05	0.0	0	0.43	0.0
Pancreas	0	0.38	0.0	1	0.25	4.1	0	0.08	0.0	0	0.09	0.0	1	0.79	1.3
Respiratory system	**1**	**2.02**	**0.5**	**0**	**1.32**	**0.0**	**0**	**0.42**	**0.0**	**2**	**0.40**	**5.0**	**3**	**4.16**	**0.7**
Nasal cavities, sinuses	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.05	0.0
Larynx	0	0.13	0.0	0	0.09	0.0	0	0.03	0.0	1	0.02	40.4	1	0.27	3.6
Trachea, bronchus, lung	1	1.78	0.6	0	1.16	0.0	0	0.37	0.0	1	0.35	2.9	2	3.65	0.5
Prostate gland	0	1.33	0.0	1	0.86	1.2	0	0.26	0.0	1	0.35	2.9	2	2.80	0.7
Testis	0	0.03	0.0	1	0.02	53.9	0	0.01	0.0	0	0.00	0.0	1	0.06	16.7
Kidney, renal pelvis, ureter	1	0.32	3.2	0	0.20	0.0	0	0.06	0.0	0	0.07	0.0	1	0.66	1.5
Bladder, other urinary	1	0.80	1.2	0	0.53	0.0	1	0.17	6.0	0	0.18	0.0	2	1.68	1.2
Melanoma of the skin	0	0.08	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.16	0.0
Eye	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Brain, central nervous system	0	0.15	0.0	0	0.10	0.0	0	0.03	0.0	1	0.03	39.8	1	0.31	3.2
Thyroid gland	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Bone	0	0.02	0.0	0	0.01	0.0	0	0.00	0.0	0	0.00	0.0	0	0.03	0.0
Connective tissue	1	0.03	32.3	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	1	0.06	16.2
Lymphatic, hematopoietic system	**0**	**0.63**	**0.0**	**0**	**0.40**	**0.0**	**0**	**0.12**	**0.0**	**0**	**0.14**	**0.0**	**0**	**1.29**	**0.0**
Non-Hodgkin's lymphoma	0	0.16	0.0	0	0.10	0.0	0	0.03	0.0	0	0.03	0.0	0	0.33	0.0
Hodgkin's disease	0	0.04	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Multiple myeloma	0	0.12	0.0	0	0.08	0.0	0	0.02	0.0	0	0.03	0.0	0	0.24	0.0
Leukemias	0	0.30	0.0	0	0.19	0.0	0	0.06	0.0	0	0.07	0.0	0	0.61	0.0
Chronic lymphocytic	0	0.17	0.0	0	0.10	0.0	0	0.03	0.0	0	0.04	0.0	0	0.34	0.0
Acute nonlymphocytic	0	0.07	0.0	0	0.05	0.0	0	0.01	0.0	0	0.02	0.0	0	0.15	0.0

[a] ICD-7 code = 155.
[b] $P < .05$.

LIVER, BILIARY FEMALES

TABLE 6E. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the liver, gallbladder, or other biliary among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,811			519			105			50			2,811		
Person-yr in interval	1,305			796			351			309			2,760		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**12**	**13.44**	**0.9**	**12**	**8.68**	**1.4**	**4**	**4.23**	**0.9**	**1**	**3.91**	**0.3**	**29**	**30.26**	**1.0**
All excluding site of initial cancer	**12**	**13.00**	**0.9**	**10**	**8.38**	**1.2**	**3**	**4.07**	**0.7**	**1**	**3.76**	**0.3**	**26**	**29.21**	**0.9**
Buccal cavity, pharynx	**0**	**0.18**	**0.0**	**0**	**0.12**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.42**	**0.0**
Lip	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Tongue	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Salivary gland	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Gum, other mouth	0	0.05	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Pharynx	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Digestive system	**4**	**4.95**	**0.8**	**6**	**3.25**	**1.8**	**2**	**1.65**	**1.2**	**0**	**1.53**	**0.0**	**12**	**11.38**	**1.1**
Esophagus	0	0.14	0.0	0	0.09	0.0	0	0.05	0.0	0	0.04	0.0	0	0.33	0.0
Stomach	0	1.28	0.0	1	0.80	1.2	0	0.39	0.0	0	0.35	0.0	1	2.82	0.4
Colon	2	1.54	1.3	2	1.04	1.9	1	0.54	1.9	0	0.51	0.0	5	3.62	1.4
Rectum	0	0.85	0.0	0	0.55	0.0	0	0.27	0.0	0	0.25	0.0	0	1.93	0.0
Liver, biliary	0	0.44	0.0	2	0.30	6.6	1	0.16	6.3	0	0.15	0.0	3	1.05	2.9
Pancreas	2	0.51	3.9	1	0.34	2.9	0	0.18	0.0	0	0.17	0.0	3	1.20	2.5
Respiratory system	**1**	**0.70**	**1.4**	**0**	**0.46**	**0.0**	**1**	**0.23**	**4.4**	**0**	**0.21**	**0.0**	**2**	**1.59**	**1.3**
Nasal cavities, sinuses	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Larynx	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Trachea, bronchus, lung	1	0.59	1.7	0	0.39	0.0	1	0.19	5.3	0	0.18	0.0	2	1.34	1.5
Female breast	2	2.67	0.7	1	1.71	0.6	0	0.82	0.0	0	0.75	0.0	3	5.95	0.5
Female genital tract	**3**	**2.30**	**1.3**	**5**	**1.42**	**3.5**[b]	**1**	**0.64**	**1.6**	**1**	**0.58**	**1.7**	**10**	**4.94**	**2.0**
Cervix uteri	0	0.65	0.0	0	0.39	0.0	0	0.16	0.0	1	0.15	6.9	1	1.34	0.7
Corpus uteri	0	0.70	0.0	3	0.43	7.0[b]	0	0.19	0.0	0	0.17	0.0	3	1.49	2.0
Uterus, NOS	0	0.06	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Ovary, fallopian tubes	3	0.73	4.1	1	0.46	2.2	1	0.21	4.8	0	0.19	0.0	5	1.58	3.2[b]
Kidney, renal pelvis, ureter	1	0.37	2.7	0	0.24	0.0	0	0.12	0.0	0	0.11	0.0	1	0.83	1.2
Bladder, other urinary	0	0.40	0.0	0	0.27	0.0	0	0.14	0.0	0	0.13	0.0	0	0.93	0.0
Melanoma of the skin	0	0.16	0.0	0	0.11	0.0	0	0.05	0.0	0	0.04	0.0	0	0.36	0.0
Eye	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Brain, central nervous system	0	0.23	0.0	0	0.15	0.0	0	0.06	0.0	0	0.06	0.0	0	0.50	0.0
Thyroid gland	1	0.09	10.5	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	1	0.22	4.6
Bone	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.04	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Lymphatic, hematopoietic system	**0**	**0.74**	**0.0**	**0**	**0.49**	**0.0**	**0**	**0.25**	**0.0**	**0**	**0.23**	**0.0**	**0**	**1.71**	**0.0**
Non-Hodgkin's lymphoma	0	0.22	0.0	0	0.15	0.0	0	0.07	0.0	0	0.07	0.0	0	0.51	0.0
Hodgkin's disease	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.11	0.0
Multiple myeloma	0	0.15	0.0	0	0.10	0.0	0	0.05	0.0	0	0.05	0.0	0	0.35	0.0
Leukemias	0	0.31	0.0	0	0.21	0.0	0	0.11	0.0	0	0.10	0.0	0	0.73	0.0
Chronic lymphocytic	0	0.14	0.0	0	0.10	0.0	0	0.05	0.0	0	0.05	0.0	0	0.34	0.0
Acute nonlymphocytic	0	0.09	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.21	0.0

[a] ICD-7 code = 155.

[b] $P < .05$.

PANCREAS
BOTH SEXES

TABLE 7A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the pancreas, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	4,169	3,583	7,752
No. who developed a second primary cancer	41	47	88
Average age at diagnosis of first cancer, yr	65	67	66
Average yr of diagnosis of first cancer	1966	1967	1966
Person-yr of follow-up	3,615	3,532	7,147
Average follow-up, yr	0.9	1.0	0.9
Percent given radiotherapy for first cancer	3	2	3

[a] ICD-7 code = 157.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 7B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the pancreas in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	46	52.3
Only the first cancer	4	4.6
Only the second cancer	26	29.6
Neither first nor second cancer	12	13.6
Total second primary cancers	88	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

PANCREAS
BOTH SEXES

TABLE 7C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pancreas among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	7,752			1,268			238			130			7,752		
Person-yr in interval	3,564			1,731			877			975			7,147		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**32**	**39.59**	**0.8**	**17**	**20.66**	**0.8**	**11**	**11.17**	**1.0**	**28**	**13.81**	**2.0**[b]	**88**	**85.23**	**1.0**
All excluding site of initial cancer	**32**	**38.07**	**0.8**	**17**	**19.85**	**0.9**	**11**	**10.73**	**1.0**	**28**	**13.23**	**2.1**[b]	**88**	**81.87**	**1.1**
Buccal cavity, pharynx	**1**	**0.96**	**1.0**	**0**	**0.48**	**0.0**	**0**	**0.25**	**0.0**	**1**	**0.28**	**3.6**	**2**	**1.97**	**1.0**
Lip	0	0.44	0.0	0	0.22	0.0	0	0.11	0.0	0	0.12	0.0	0	0.88	0.0
Tongue	0	0.09	0.0	0	0.05	0.0	0	0.02	0.0	0	0.03	0.0	0	0.20	0.0
Salivary gland	0	0.11	0.0	0	0.05	0.0	0	0.03	0.0	1	0.04	25.0	1	0.22	4.5
Gum, other mouth	0	0.17	0.0	0	0.09	0.0	0	0.05	0.0	0	0.06	0.0	0	0.37	0.0
Pharynx	1	0.15	6.7	0	0.08	0.0	0	0.04	0.0	0	0.04	0.0	1	0.31	3.2
Digestive system	**12**	**14.71**	**0.8**	**6**	**7.83**	**0.8**	**2**	**4.22**	**0.5**	**6**	**5.15**	**1.2**	**26**	**31.92**	**0.8**
Esophagus	0	0.55	0.0	0	0.29	0.0	0	0.15	0.0	0	0.18	0.0	0	1.18	0.0
Stomach	3	4.26	0.7	1	2.26	0.4	0	1.18	0.0	1	1.33	0.8	5	9.04	0.6
Colon	4	3.86	1.0	3	2.10	1.4	2	1.16	1.7	4	1.51	2.6	13	8.63	1.5
Rectum	2	2.99	0.7	0	1.57	0.0	0	0.83	0.0	1	0.99	1.0	3	6.38	0.5
Liver, biliary	1	1.00	1.0	2	0.54	3.7	0	0.31	0.0	0	0.41	0.0	3	2.26	1.3
Pancreas	0	1.52	0.0	0	0.81	0.0	0	0.44	0.0	0	0.58	0.0	0	3.36	0.0
Respiratory system	**1**	**5.57**	**0.2**[b]	**1**	**2.71**	**0.4**	**0**	**1.43**	**0.0**	**4**	**1.76**	**2.3**	**6**	**11.47**	**0.5**
Nasal cavities, sinuses	0	0.09	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.19	0.0
Larynx	0	0.35	0.0	0	0.17	0.0	0	0.09	0.0	1	0.10	10.0	1	0.70	1.4
Trachea, bronchus, lung	1	4.85	0.2	1	2.34	0.4	0	1.24	0.0	3	1.54	1.9	5	9.97	0.5
Female breast	1	3.34	0.3	2	1.74	1.2	3	0.96	3.1	3	1.35	2.2	9	7.39	1.2
Female genital tract	**5**	**2.89**	**1.7**	**1**	**1.48**	**0.7**	**2**	**0.82**	**2.5**	**8**	**1.06**	**7.6**[b]	**16**	**6.25**	**2.6**[b]
Cervix uteri	0	0.84	0.0	1	0.43	2.3	0	0.24	0.0	3	0.28	10.7[b]	4	1.79	2.2
Corpus uteri	1	0.87	1.2	0	0.44	0.0	2	0.24	8.5	3	0.32	9.5[b]	6	1.85	3.2[b]
Uterus, NOS	0	0.07	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.16	0.0
Ovary, fallopian tubes	4	0.90	4.4[b]	0	0.46	0.0	0	0.26	0.0	2	0.35	5.8	6	1.96	3.1[b]
Prostate gland	3	3.14	1.0	0	1.77	0.0	2	0.98	2.0	1	1.10	0.9	6	6.99	0.9
Testis	1	0.08	13.2	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	1	0.14	7.1
Kidney, renal pelvis, ureter	3	1.20	2.5	2	0.63	3.2	0	0.33	0.0	2	0.41	4.9	7	2.57	2.7[b]
Bladder, other urinary	3	2.35	1.3	3	1.21	2.5	1	0.67	1.5	0	0.82	0.0	7	5.05	1.4
Melanoma of the skin	0	0.38	0.0	0	0.19	0.0	0	0.11	0.0	0	0.14	0.0	0	0.82	0.0
Eye	0	0.11	0.0	0	0.05	0.0	0	0.03	0.0	1	0.04	25.0	1	0.24	4.2
Brain, central nervous system	0	0.66	0.0	0	0.32	0.0	0	0.16	0.0	0	0.20	0.0	0	1.34	0.0
Thyroid gland	0	0.19	0.0	0	0.09	0.0	0	0.06	0.0	0	0.07	0.0	0	0.40	0.0
Bone	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.14	0.0
Connective tissue	0	0.13	0.0	1	0.07	14.3	0	0.04	0.0	0	0.04	0.0	1	0.26	3.8
Lymphatic, hematopoietic system	**1**	**2.40**	**0.4**	**0**	**1.26**	**0.0**	**0**	**0.69**	**0.0**	**2**	**0.85**	**2.4**	**3**	**5.20**	**0.6**
Non-Hodgkin's lymphoma	0	0.65	0.0	0	0.34	0.0	0	0.18	0.0	0	0.23	0.0	0	1.40	0.0
Hodgkin's disease	1	0.16	6.3	0	0.08	0.0	0	0.04	0.0	0	0.05	0.0	1	0.34	2.9
Multiple myeloma	0	0.47	0.0	0	0.25	0.0	0	0.14	0.0	0	0.17	0.0	0	1.02	0.0
Leukemias	0	1.09	0.0	0	0.59	0.0	0	0.32	0.0	2	0.39	5.1	2	2.39	0.8
Chronic lymphocytic	0	0.58	0.0	0	0.30	0.0	0	0.17	0.0	1	0.20	5.0	1	1.26	0.8
Acute nonlymphocytic	0	0.28	0.0	0	0.15	0.0	0	0.08	0.0	1	0.11	9.1	1	0.61	1.6

[a] ICD-7 code = 157.

[b] $P < .05$.

PANCREAS
MALES

TABLE 7D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pancreas among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	4,169			674			120			60			4,169		
Person-yr in interval	1,915			881			418			402			3,615		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**16**	**22.93**	**0.7**	**8**	**11.90**	**0.7**	**6**	**6.27**	**1.0**	**11**	**6.95**	**1.6**	**41**	**48.05**	**0.9**
All excluding site of initial cancer	**16**	**22.03**	**0.7**	**8**	**11.43**	**0.7**	**6**	**6.02**	**1.0**	**11**	**6.66**	**1.7**	**41**	**46.14**	**0.9**
Buccal cavity, pharynx	**0**	**0.73**	**0.0**	**0**	**0.36**	**0.0**	**0**	**0.18**	**0.0**	**1**	**0.19**	**5.1**	**1**	**1.46**	**0.7**
Lip	0	0.40	0.0	0	0.20	0.0	0	0.10	0.0	0	0.11	0.0	0	0.80	0.0
Tongue	0	0.05	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.11	0.0
Salivary gland	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	1	0.02	62.9	1	0.12	8.3
Gum, other mouth	0	0.10	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.21	0.0
Pharynx	0	0.11	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.23	0.0
Digestive system	**7**	**8.63**	**0.8**	**1**	**4.57**	**0.2**	**2**	**2.38**	**0.8**	**2**	**2.55**	**0.8**	**12**	**18.14**	**0.7**
Esophagus	0	0.38	0.0	0	0.20	0.0	0	0.10	0.0	0	0.10	0.0	0	0.78	0.0
Stomach	1	2.71	0.4	0	1.44	0.0	0	0.73	0.0	1	0.74	1.4	2	5.62	0.4
Colon	3	1.96	1.5	1	1.07	0.9	2	0.57	3.5	1	0.64	1.6	7	4.24	1.7
Rectum	1	1.94	0.5	0	1.01	0.0	0	0.52	0.0	0	0.56	0.0	1	4.03	0.2
Liver, biliary	1	0.47	2.1	0	0.25	0.0	0	0.14	0.0	0	0.16	0.0	1	1.02	1.0
Pancreas	0	0.90	0.0	0	0.47	0.0	0	0.25	0.0	0	0.29	0.0	0	1.91	0.0
Respiratory system	**1**	**4.70**	**0.2**	**1**	**2.27**	**0.4**	**0**	**1.18**	**0.0**	**3**	**1.39**	**2.2**	**5**	**9.54**	**0.5**
Nasal cavities, sinuses	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Larynx	0	0.32	0.0	0	0.15	0.0	0	0.08	0.0	1	0.09	11.2	1	0.63	1.6
Trachea, bronchus, lung	1	4.12	0.2	1	1.97	0.5	0	1.03	0.0	2	1.22	1.6	4	8.34	0.5
Prostate gland	3	3.14	1.0	0	1.77	0.0	2	0.98	2.0	1	1.10	0.9	6	6.99	0.9
Testis	1	0.08	13.2	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	1	0.14	7.1
Kidney, renal pelvis, ureter	1	0.75	1.3	2	0.39	5.2	0	0.20	0.0	2	0.22	9.0[b]	5	1.56	3.2[b]
Bladder, other urinary	2	1.86	1.1	2	0.95	2.1	1	0.52	1.9	0	0.60	0.0	5	3.93	1.3
Melanoma of the skin	0	0.18	0.0	0	0.09	0.0	0	0.05	0.0	0	0.05	0.0	0	0.37	0.0
Eye	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.14	0.0
Brain, central nervous system	0	0.37	0.0	0	0.17	0.0	0	0.08	0.0	0	0.09	0.0	0	0.71	0.0
Thyroid gland	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Bone	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Connective tissue	0	0.08	0.0	1	0.04	25.8	0	0.02	0.0	0	0.02	0.0	1	0.15	6.5
Lymphatic, hematopoietic system	**1**	**1.49**	**0.7**	**0**	**0.78**	**0.0**	**0**	**0.41**	**0.0**	**2**	**0.45**	**4.4**	**3**	**3.13**	**1.0**
Non-Hodgkin's lymphoma	0	0.38	0.0	0	0.20	0.0	0	0.10	0.0	0	0.11	0.0	0	0.79	0.0
Hodgkin's disease	1	0.10	9.6	0	0.05	0.0	0	0.02	0.0	0	0.03	0.0	1	0.21	4.9
Multiple myeloma	0	0.28	0.0	0	0.15	0.0	0	0.08	0.0	0	0.09	0.0	0	0.59	0.0
Leukemias	0	0.71	0.0	0	0.38	0.0	0	0.20	0.0	2	0.22	9.1[b]	2	1.51	1.3
Chronic lymphocytic	0	0.40	0.0	0	0.21	0.0	0	0.11	0.0	1	0.12	8.1	1	0.85	1.2
Acute nonlymphocytic	0	0.17	0.0	0	0.09	0.0	0	0.05	0.0	1	0.06	17.7	1	0.36	2.8

[a] ICD-7 code = 157.

[b] $P < .05$.

PANCREAS
FEMALES

TABLE 7E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the pancreas among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,583			594			118			70			3,583		
Person-yr in interval	1,649			850			460			573			3,532		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**16**	**16.66**	**1.0**	**9**	**8.76**	**1.0**	**5**	**4.90**	**1.0**	**17**	**6.86**	**2.5**[b]	**47**	**37.18**	**1.3**
All excluding site of initial cancer	**16**	**16.04**	**1.0**	**9**	**8.42**	**1.1**	**5**	**4.71**	**1.1**	**17**	**6.57**	**2.6**[b]	**47**	**35.73**	**1.3**
Buccal cavity, pharynx	**1**	**0.23**	**4.3**	**0**	**0.12**	**0.0**	**0**	**0.07**	**0.0**	**0**	**0.09**	**0.0**	**1**	**0.51**	**1.9**
Lip	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Tongue	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.09	0.0
Salivary gland	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.10	0.0
Gum, other mouth	0	0.07	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.16	0.0
Pharynx	1	0.04	25.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	1	0.08	11.9
Digestive system	**5**	**6.08**	**0.8**	**5**	**3.26**	**1.5**	**0**	**1.84**	**0.0**	**4**	**2.60**	**1.5**	**14**	**13.78**	**1.0**
Esophagus	0	0.17	0.0	0	0.09	0.0	0	0.05	0.0	0	0.08	0.0	0	0.40	0.0
Stomach	2	1.55	1.3	1	0.82	1.2	0	0.45	0.0	0	0.59	0.0	3	3.42	0.9
Colon	1	1.90	0.5	2	1.03	1.9	0	0.59	0.0	3	0.87	3.5	6	4.39	1.4
Rectum	1	1.05	1.0	0	0.56	0.0	0	0.31	0.0	1	0.43	2.3	2	2.35	0.8
Liver, biliary	0	0.53	0.0	2	0.29	6.9	0	0.17	0.0	0	0.25	0.0	2	1.24	1.6
Pancreas	0	0.62	0.0	0	0.34	0.0	0	0.19	0.0	0	0.29	0.0	0	1.45	0.0
Respiratory system	**0**	**0.87**	**0.0**	**0**	**0.44**	**0.0**	**0**	**0.25**	**0.0**	**1**	**0.37**	**2.7**	**1**	**1.93**	**0.5**
Nasal cavities, sinuses	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Larynx	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Trachea, bronchus, lung	0	0.73	0.0	0	0.37	0.0	0	0.21	0.0	1	0.32	3.2	1	1.63	0.6
Female breast	1	3.34	0.3	2	1.74	1.2	3	0.96	3.1	3	1.35	2.2	9	7.39	1.2
Female genital tract	**5**	**2.89**	**1.7**	**1**	**1.48**	**0.7**	**2**	**0.82**	**2.5**	**8**	**1.06**	**7.6**[b]	**16**	**6.25**	**2.6**[b]
Cervix uteri	0	0.84	0.0	1	0.43	2.3	0	0.24	0.0	3	0.28	10.7[b]	4	1.79	2.2
Corpus uteri	1	0.87	1.2	0	0.44	0.0	2	0.24	8.5	3	0.32	9.5[b]	6	1.85	3.2[b]
Uterus, NOS	0	0.07	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.16	0.0
Ovary, fallopian tubes	4	0.90	4.4[b]	0	0.46	0.0	0	0.26	0.0	2	0.35	5.8	6	1.96	3.1[b]
Kidney, renal pelvis, ureter	2	0.45	4.5	0	0.24	0.0	0	0.13	0.0	0	0.19	0.0	2	1.01	2.0
Bladder, other urinary	1	0.49	2.0	1	0.26	3.8	0	0.15	0.0	0	0.22	0.0	2	1.12	1.8
Melanoma of the skin	0	0.20	0.0	0	0.10	0.0	0	0.06	0.0	0	0.09	0.0	0	0.45	0.0
Eye	0	0.04	0.0	0	0.02	0.0	0	0.01	0.0	1	0.02	59.4	1	0.10	10.2
Brain, central nervous system	0	0.29	0.0	0	0.15	0.0	0	0.08	0.0	0	0.11	0.0	0	0.63	0.0
Thyroid gland	0	0.12	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.27	0.0
Bone	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Connective tissue	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**0**	**0.91**	**0.0**	**0**	**0.48**	**0.0**	**0**	**0.28**	**0.0**	**0**	**0.40**	**0.0**	**0**	**2.07**	**0.0**
Non-Hodgkin's lymphoma	0	0.27	0.0	0	0.14	0.0	0	0.08	0.0	0	0.12	0.0	0	0.61	0.0
Hodgkin's disease	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.13	0.0
Multiple myeloma	0	0.19	0.0	0	0.10	0.0	0	0.06	0.0	0	0.08	0.0	0	0.43	0.0
Leukemias	0	0.38	0.0	0	0.21	0.0	0	0.12	0.0	0	0.17	0.0	0	0.88	0.0
Chronic lymphocytic	0	0.18	0.0	0	0.09	0.0	0	0.06	0.0	0	0.08	0.0	0	0.41	0.0
Acute nonlymphocytic	0	0.11	0.0	0	0.06	0.0	0	0.03	0.0	0	0.05	0.0	0	0.25	0.0

[a] ICD-7 code = 157.

[b] $P < .05$.

Second Cancer Following Cancer of the Respiratory System in Denmark, 1943–80 [1]

Jørgen H. Olsen [2, 3]

ABSTRACT—A 10% increased risk of developing a second cancer was observed among approximately 36,000 persons reported to the Danish Cancer Registry with a cancer of the respiratory system during 1943-80. This estimate is markedly influenced by a striking tendency by physicians not to report or the Cancer Registry not to accept a report of a second lung cancer following a primary lung cancer (14 observed vs. 99 expected). A significant 30% excess of all second cancers was seen after laryngeal cancer (368 vs. 282), whereas the 22% excess following cancer of the nasal cavities and paranasal sinuses did not quite reach the level of statistical significance (95% CI = 0.9-1.6). For cancers of the lung and larynx, second cancers arose mainly in the buccal cavity, bladder, kidney (after lung cancer only) and lung (after laryngeal cancer only). These second cancers may be due to common carcinogenic factors, most likely tobacco. Elevated risks of second cancers of the breast, cervix uteri, and other female genital organs were found consistently. Radiotherapy may have contributed to the increased risk of breast cancer, but the excess risk of cancer of the female genital organs other than the cervix was unexpected. Although not significant, the risk of esophageal cancer following cancer of the larynx was below expectation (1 vs. 4.1), which was surprising because alcohol consumption and smoking are thought to be common risk factors for these 2 sites. Significant excesses of pancreatic cancer were observed following cancers of the lung, larynx, and nasal cavities, which might be due to more careful medical surveillance of these patients or to common risk factors such as cigarette smoking. Finally, the risk of a patient developing liver cancer after lung cancer was significantly elevated (22 vs. 11.6). This increase is unlikely to be due to misdiagnosed metastases from the lung, inasmuch as the risk was generally elevated throughout the observation period.—Natl Cancer Inst Monogr 68: 309-324, 1985.

LUNG (ICD-7, 162.0, 162.1)

In Denmark, lung cancer is the most common cancer among males and the fourth leading cancer among females, accounting for 19% and 6% of all male and female cancers in 1978–80, respectively (*1*). Men are 3.5 times as likely to develop lung cancer as women, and the age-standardized incidence rate for males is 57/100,000 and 16/100,000 for females. Since 1943, lung cancer increased at an average annual rate of 13% in males until about 1965 and then leveled off, whereas in females the average increase was 12% per year with a marked acceleration since 1960 (*2*). The incidence rate of lung cancer in Copenhagen is more than twice the rate observed in rural areas. In Copenhagen, the age-standardized rate of lung cancer is 82 cases/100,000 male inhabitants; lung cancer accounts for 25% of all cancers seen in this highly urban area (*3*).

Cigarette smoking is the major single cause of lung cancer in Denmark like elsewhere in the world, but industrial exposures (e.g., asbestos, radiation, chromium, nickel, polycyclic hydrocarbons) and air pollution have also been implicated as contributory factors (*4*). A Danish study has shown that most, but not all, of the variation in lung cancer incidence between urban and rural areas can be attributed to differences in smoking habits (*5*). The case fatality rate following lung cancer is high, and the 5-year relative survival rate is only 7–8% (*6*).

Results

During 1943–80, the Registry received reports on 31,047 persons with a cancer of the trachea, bronchus, or lung who fulfilled the criteria for inclusion in the study. Eighty-two percent were males. The average age at diagnosis was 64 years for males and 63 years for females. The average follow-up was only 1.5 years. The average year of diagnosis was 1968. Radiation was given to 24% of the patients with lung cancer as part of their initial treatment.

Altogether, 400 (or 1.6%) of the male and 95 (or 1.7%) of the female patients with lung cancer developed a second primary cancer. The 495 second cancers can be compared with 509 expected on the basis of cancer incidence rates in the general population (RR = 0.97; 95% CI = 0.89–1.06). A total of 440 cases were expected among males (RR = 0.9; 95% CI = 0.8–1.0) and 69 among females (RR = 1.4; 95% CI = 1.1–1.7). Second lung cancers were substantially underreported, inasmuch as only 14 were recorded versus 99.2 expected. When second lung cancer cases were excluded from the analysis, 481 second primary cancers remained compared with 409.7 expected (RR = 1.17; 95% CI = 1.07–1.28).

Cancers of the bladder (RR = 1.6), kidney (RR = 2.7), larynx (RR = 3.1), and liver (RR = 1.9) were significantly increased following an initial diagnosis of lung cancer. Among females, significant excesses were found for cancers of the buccal cavity (RR = 4.5), pancreas (RR

ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; RR = relative risk(s); CI = confidence interval.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Jørgen H. Olsen, M.D.

[3] The valuable comments of Dr. H. Høi Hansen, Department of Oncology II, Finsen Institute, Copenhagen, are greatly appreciated.

= 2.8), and female genital organs (RR = 1.7). The risk of developing a second cancer in the female genital organs rose significantly with time since the lung cancer was diagnosed ($P < .001$ for trend), as did the risk for cancer of the breast ($P < .02$). Among males, significant excesses were seen for cancers of the liver (RR = 2.0), larynx (RR = 3.2), kidney (RR = 2.7), and bladder (RR = 1.6).

Discussion

A 38% excess risk of second primary cancer following lung cancer was observed among females, whereas the overall risk among males seemed to be 9% below expectation. The risk of a second lung cancer, however, was far below that expected and was especially low among males. Undoubtedly, this low risk is an artifact of tumor registration practice whereby multiple tumors in paired organs are entered only once in the Registry, unless the tumors are of different histologic types (*7*). When lung cancers are excluded from the analysis, the overall RR of developing a second cancer became 1.44 and 1.12 among females and males, respectively.

Most of the cancers found to be in excess were tobacco related, i.e., buccal cavity, bladder, and larynx (*8, 9*). These findings are in line with previous investigations of second primary cancer following cancer of the lung (*10–13*). A proportion of the excess cancers of the liver and kidney may be misdiagnosed metastatic lesions; however, no excess cancer risk was found in other organs where metastatic dissemination of lung cancer is often seen, such as the adrenal gland, brain, and bone. Interestingly, both cancers of the liver and kidney have recently been associated with smoking cigarettes (*14, 15*).

For reasons that are unclear, second tumors of all female genital organs occurred significantly above expectation, and the RR increased over time since the lung cancer diagnosis. Cancer of the cervix uteri has been associated with smoking (*16*) and lower socioeconomic status, which is similar to lung cancer (*17, 18*). Cancer of the uterine corpus, however, has not been linked to smoking or low social class and was equally increased. A positive trend with time was also found for cancer of the breast, which may reflect an effect of radiation treatment given for the first tumor. Breast tissue is known to be sensitive to the carcinogenic action of radiation (*19*), and radiotherapy was given to 23% of the women with lung cancer. The significant excess of pancreatic cancer among females was not seen in males and might be due to chance or possibly smoking (*20–22*).

LARYNX (ICD-7, 161)

Cancer of the larynx accounts for 1% of all cancer cases in Denmark (*1*). The age-standardized incidence rates are 5.4/100,000 for males and 0.8/100,000 for females. During the period 1943–80, an average annual increase of 6% was observed in males, but no clear trend was seen among females (*2*). The 5-year relative survival rates in Denmark are 66% (*6*). Several studies have reported that tobacco smoking and heavy alcohol consumption, in particular hard liquor, increases the risk of laryngeal cancer, and that together they may interact in a multiplicative fashion (*23, 24*). Asbestos exposure has been suggested to increase the risk of laryngeal cancer as have certain other occupational agents (*25*).

Results

A total of 3,847 persons with cancer of the larynx who survived more than 2 months without developing a new cancer were reported to the Registry between 1943 and 1980 and are included in this analysis. Second primary cancers developed in 9.6% of these persons (RR = 1.3; 95% CI = 1.1–1.4 for males; and RR = 1.6; 95% CI = 1.2–2.1 for females). The average age of diagnosis was 63 years, and the average follow-up was 6.0 years. The average year of diagnosis was 1967. Radiation therapy was given to 90% of the patients with laryngeal cancers.

Cancer of the lung was the predominant second cancer and accounted for 36% of all second cancers (RR = 2.6; 95% CI = 2.2–3.1). This increased risk was seen during the first years of follow-up and throughout the entire observation period. The risk of a subsequent cancer in the buccal cavity was significantly elevated (RR = 2.0), whereas the risk of cancer of the esophagus was reduced although not significantly (1 observed, 4.1 expected). Excess risks of borderline significance were seen for cancers of the bladder (RR = 1.4; 95% CI = 0.9–1.9), female breast (1.8; 95% CI = 0.9–3.2), and cervix uteri (3.0; 95% CI = 1.0–6.9). Among males, more second pancreatic cancers were seen than expected (RR = 1.8; 95% CI = 1.0–2.8). A positive trend over time was observed for cancers of the bladder ($P = .017$) and breast ($P < .001$). No sites occurred significantly below expectation.

Discussion

Persons with laryngeal cancer have a relatively good 5-year survival experience but are at a significant 30% increased risk of developing a subsequent cancer when compared with the population in general. About 10% of all patients with laryngeal cancer developed a new cancer.

Most of the excess of second cancers (lung, bladder, and buccal cavity) are undoubtedly due to an above average tobacco use, although occupational exposure could also be involved. As alcohol and tobacco in combination are common risk factors for cancers of the larynx (at least supraglottic cancer) and the esophagus, it is noteworthy that esophageal cancer was not increased. The risk of pancreatic cancer was significantly elevated but only among males and might be due to chance, intense medical surveillance, or smoking habits (*20–22*). Although breast cancer was not significantly elevated, the RR increased with time since diagnosis. The question of whether radiotherapy might be responsible for this increase should be investigated.

NASAL CAVITIES AND PARANASAL SINUSES (ICD-7, 160)

Cancer of the nasal cavities and paranasal sinuses account for only a small fraction of all cancers in Denmark (*1*). The age-standardized incidence rates are 0.9 and 0.5/100,000 for males and females, respectively (*2*).

Throughout 1943–80, the increase in incidence of these tumors has been 6–7%, but only among males (*26*). The 5-year relative survival rates are approximately 40% (*6*). Elevated risks for sinonasal cancer have been associated with occupational exposures to nickel (*27*), wood dust (*28*), chromates (*29*), and leather dust (*30*). Recently, it has also been suggested that formaldehyde and cigarette smoking might increase the risk of cancer of these sites (*31, 32*).

Results

Among 1,062 persons with cancer of the nasal cavities and paranasal sinuses, 58 (or 5.5%) developed a second cancer (RR = 1.22; 95% CI = 0.93–1.58). The average age at diagnosis was 63 years, and the average follow-up was 4.5 years. The average year of diagnosis was 1965. Two of every 3 cancers occurred in males. Radiotherapy was received by 79% of the patients as part of their initial treatment.

An increased lung cancer risk was observed but only among males (RR = 2.0; 95% CI = 1.0–3.5). The RR of bladder cancer (2.3) and leukemia (3.2) in males and cancers of the breast (1.7) and pancreas (6.1) in females were above expectation, but the numbers of cancers were small and only pancreatic cancer in females was significantly increased. The overall risks of developing any second cancer were slightly elevated in all follow-up intervals among males but not among females.

Discussion

A 22% elevated risk of developing a second cancer was observed among patients with sinonasal cancer. The specific sites of cancer excess were the lung, bladder, and leukemia among males, and the breast and pancreas among females. Although these findings could lend some support to recent suggestions of an etiologic role for tobacco in nasal cavity tumors (*32*), our numbers are small and chance cannot be excluded as an explanation for these findings.

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NASAL CAVITIES
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the nasal cavities or sinuses, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	702	360	1,062
No. who developed a second primary cancer	41	17	58
Average age at diagnosis of first cancer, yr	63	62	63
Average yr of diagnosis of first cancer	1965	1964	1965
Person-yr of follow-up	2,735	1,900	4,635
Average follow-up, yr	3.9	5.3	4.5
Percent given radiotherapy for first cancer	80	79	79

[a] ICD-7 code = 160.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the nasal cavities or sinuses in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	41	70.7
Only the first cancer	9	15.5
Only the second cancer	6	10.3
Neither first nor second cancer	2	3.5
Total second primary cancers	58	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

NASAL CAVITIES
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the nasal cavities or sinuses among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,062			695			288			143			1,062		
Person-yr in interval	892			1,678			1,008			1,057			4,634		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8**	**8.81**	**0.9**	**26**	**16.98**	**1.5**	**11**	**10.18**	**1.1**	**13**	**11.43**	**1.1**	**58**	**47.38**	**1.2**
All excluding site of initial cancer	**8**	**8.78**	**0.9**	**26**	**16.94**	**1.5**[b]	**11**	**10.15**	**1.1**	**13**	**11.40**	**1.1**	**58**	**47.27**	**1.2**
Buccal cavity, pharynx	**0**	**0.24**	**0.0**	**0**	**0.44**	**0.0**	**0**	**0.24**	**0.0**	**0**	**0.26**	**0.0**	**0**	**1.17**	**0.0**
Lip	0	0.12	0.0	0	0.20	0.0	0	0.11	0.0	0	0.11	0.0	0	0.54	0.0
Tongue	0	0.03	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.11	0.0
Salivary gland	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Gum, other mouth	0	0.04	0.0	0	0.07	0.0	0	0.05	0.0	0	0.05	0.0	0	0.21	0.0
Pharynx	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.04	0.0	0	0.19	0.0
Digestive system	**4**	**3.33**	**1.2**	**7**	**6.11**	**1.1**	**5**	**3.51**	**1.4**	**3**	**3.91**	**0.8**	**19**	**16.85**	**1.1**
Esophagus	0	0.14	0.0	0	0.23	0.0	0	0.13	0.0	0	0.14	0.0	0	0.64	0.0
Stomach	2	1.04	1.9	1	1.72	0.6	3	0.91	3.3	0	0.93	0.0	6	4.60	1.3
Colon	1	0.81	1.2	4	1.62	2.5	1	0.97	1.0	1	1.15	0.9	7	4.56	1.5
Rectum	0	0.69	0.0	1	1.26	0.8	0	0.72	0.0	1	0.78	1.3	2	3.45	0.6
Liver, biliary	0	0.20	0.0	0	0.42	0.0	0	0.26	0.0	0	0.32	0.0	0	1.20	0.0
Pancreas	1	0.33	3.0	1	0.66	1.5	1	0.40	2.5	1	0.47	2.1	4	1.85	2.2
Respiratory system	**3**	**1.33**	**2.3**	**3**	**2.66**	**1.1**	**3**	**1.64**	**1.8**	**3**	**1.75**	**1.7**	**12**	**7.37**	**1.6**
Nasal cavities, sinuses	0	0.03	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Larynx	0	0.10	0.0	0	0.17	0.0	0	0.11	0.0	0	0.11	0.0	0	0.48	0.0
Trachea, bronchus, lung	3	1.15	2.6	2	2.32	0.9	3	1.44	2.1	3	1.54	1.9	11	6.43	1.7
Female breast	0	0.54	0.0	3	1.17	2.6	0	0.82	0.0	3	1.04	2.9	6	3.57	1.7
Female genital tract	**0**	**0.49**	**0.0**	**1**	**1.05**	**1.0**	**0**	**0.72**	**0.0**	**1**	**0.89**	**1.1**	**2**	**3.14**	**0.6**
Cervix uteri	0	0.16	0.0	0	0.34	0.0	0	0.22	0.0	0	0.25	0.0	0	0.97	0.0
Corpus uteri	0	0.14	0.0	0	0.30	0.0	0	0.21	0.0	0	0.27	0.0	0	0.92	0.0
Uterus, NOS	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Ovary, fallopian tubes	0	0.15	0.0	1	0.31	3.2	0	0.22	0.0	1	0.28	3.5	2	0.96	2.1
Prostate gland	1	0.83	1.2	2	1.56	1.3	1	0.83	1.2	0	0.88	0.0	4	4.10	1.0
Testis	0	0.03	0.0	1	0.05	21.1	0	0.03	0.0	0	0.03	0.0	1	0.13	7.7
Kidney, renal pelvis, ureter	0	0.27	0.0	0	0.53	0.0	0	0.32	0.0	1	0.36	2.8	1	1.48	0.7
Bladder, other urinary	0	0.56	0.0	4	1.11	3.6	2	0.67	3.0	0	0.74	0.0	6	3.08	1.9
Melanoma of the skin	0	0.08	0.0	1	0.17	5.9	0	0.11	0.0	1	0.13	7.7	2	0.50	4.0
Eye	0	0.03	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.14	0.0
Brain, central nervous system	0	0.15	0.0	0	0.30	0.0	0	0.18	0.0	0	0.21	0.0	0	0.85	0.0
Thyroid gland	0	0.04	0.0	0	0.07	0.0	0	0.05	0.0	0	0.06	0.0	0	0.21	0.0
Bone	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Connective tissue	0	0.03	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.15	0.0
Lymphatic, hematopoietic system	**0**	**0.54**	**0.0**	**3**	**1.05**	**2.9**	**0**	**0.63**	**0.0**	**1**	**0.72**	**1.4**	**4**	**2.94**	**1.4**
Non-Hodgkin's lymphoma	0	0.14	0.0	0	0.28	0.0	0	0.17	0.0	0	0.20	0.0	0	0.81	0.0
Hodgkin's disease	0	0.04	0.0	0	0.08	0.0	0	0.04	0.0	0	0.05	0.0	0	0.22	0.0
Multiple myeloma	0	0.10	0.0	0	0.20	0.0	0	0.12	0.0	1	0.14	7.1	1	0.56	1.8
Leukemias	0	0.25	0.0	3	0.48	6.2[b]	0	0.28	0.0	0	0.31	0.0	3	1.33	2.3
Chronic lymphocytic	0	0.14	0.0	1	0.26	3.8	0	0.14	0.0	0	0.15	0.0	1	0.69	1.4
Acute nonlymphocytic	0	0.06	0.0	1	0.13	7.7	0	0.08	0.0	0	0.09	0.0	1	0.35	2.9

[a] ICD-7 code = 160.
[b] $P < .05$.

NASAL CAVITIES
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the nasal cavities or sinuses among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	702			443			171			78			702		
Person-yr in interval	583			1,039			572			540			2,735		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**7**	**6.17**	**1.1**	**18**	**11.36**	**1.6**	**9**	**6.21**	**1.5**	**7**	**6.30**	**1.1**	**41**	**30.03**	**1.4**
All excluding site of initial cancer	**7**	**6.15**	**1.1**	**18**	**11.33**	**1.6**	**9**	**6.19**	**1.5**	**7**	**6.28**	**1.1**	**41**	**29.95**	**1.4**
Buccal cavity, pharynx	**0**	**0.20**	**0.0**	**0**	**0.36**	**0.0**	**0**	**0.19**	**0.0**	**0**	**0.19**	**0.0**	**0**	**0.94**	**0.0**
Lip	0	0.11	0.0	0	0.19	0.0	0	0.10	0.0	0	0.10	0.0	0	0.50	0.0
Tongue	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.07	0.0
Salivary gland	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Gum, other mouth	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.14	0.0
Pharynx	0	0.03	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.15	0.0
Digestive system	**3**	**2.39**	**1.3**	**4**	**4.16**	**1.0**	**3**	**2.13**	**1.4**	**2**	**2.11**	**0.9**	**12**	**10.79**	**1.1**
Esophagus	0	0.11	0.0	0	0.18	0.0	0	0.09	0.0	0	0.09	0.0	0	0.47	0.0
Stomach	2	0.78	2.6	0	1.25	0.0	2	0.59	3.4	0	0.55	0.0	4	3.17	1.3
Colon	1	0.53	1.9	3	0.99	3.0	1	0.52	1.9	1	0.54	1.8	6	2.58	2.3
Rectum	0	0.53	0.0	1	0.92	1.1	0	0.48	0.0	1	0.47	2.1	2	2.40	0.8
Liver, biliary	0	0.12	0.0	0	0.24	0.0	0	0.13	0.0	0	0.14	0.0	0	0.64	0.0
Pancreas	0	0.24	0.0	0	0.45	0.0	0	0.25	0.0	0	0.26	0.0	0	1.19	0.0
Respiratory system	**3**	**1.20**	**2.5**	**2**	**2.37**	**0.8**	**3**	**1.43**	**2.1**	**3**	**1.45**	**2.1**	**11**	**6.44**	**1.7**
Nasal cavities, sinuses	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Larynx	0	0.09	0.0	0	0.16	0.0	0	0.10	0.0	0	0.10	0.0	0	0.44	0.0
Trachea, bronchus, lung	3	1.04	2.9	2	2.07	1.0	3	1.26	2.4	3	1.28	2.4	11	5.64	2.0
Prostate gland	1	0.83	1.2	2	1.56	1.3	1	0.83	1.2	0	0.88	0.0	4	4.10	1.0
Testis	0	0.03	0.0	1	0.05	21.1	0	0.03	0.0	0	0.03	0.0	1	0.13	7.7
Kidney, renal pelvis, ureter	0	0.20	0.0	0	0.38	0.0	0	0.21	0.0	1	0.22	4.5	1	1.01	1.0
Bladder, other urinary	0	0.49	0.0	4	0.95	4.2[b]	2	0.55	3.6	0	0.58	0.0	6	2.57	2.3
Melanoma of the skin	0	0.05	0.0	1	0.10	9.8	0	0.06	0.0	0	0.06	0.0	1	0.27	3.7
Eye	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Brain, central nervous system	0	0.10	0.0	0	0.19	0.0	0	0.11	0.0	0	0.11	0.0	0	0.52	0.0
Thyroid gland	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.10	0.0
Lymphatic, hematopoietic system	**0**	**0.40**	**0.0**	**3**	**0.75**	**4.0**	**0**	**0.41**	**0.0**	**1**	**0.42**	**2.4**	**4**	**1.98**	**2.0**
Non-Hodgkin's lymphoma	0	0.10	0.0	0	0.19	0.0	0	0.11	0.0	0	0.11	0.0	0	0.52	0.0
Hodgkin's disease	0	0.03	0.0	0	0.06	0.0	0	0.03	0.0	0	0.03	0.0	0	0.15	0.0
Multiple myeloma	0	0.07	0.0	0	0.14	0.0	0	0.08	0.0	1	0.08	12.8	1	0.37	2.7
Leukemias	0	0.19	0.0	3	0.35	8.5[b]	0	0.19	0.0	0	0.19	0.0	3	0.93	3.2
Chronic lymphocytic	0	0.11	0.0	1	0.20	5.1	0	0.10	0.0	0	0.10	0.0	1	0.51	2.0
Acute nonlymphocytic	0	0.04	0.0	1	0.09	11.6	0	0.05	0.0	0	0.05	0.0	1	0.23	4.3

[a] ICD-7 code = 160.

[b] $P < .05$.

NASAL CAVITIES
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the nasal cavities or sinuses among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	360			252			117			65			360		
Person-yr in interval	309			639			435			517			1,900		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1**	**2.64**	**0.4**	**8**	**5.62**	**1.4**	**2**	**3.97**	**0.5**	**6**	**5.13**	**1.2**	**17**	**17.35**	**1.0**
All excluding site of initial cancer	**1**	**2.63**	**0.4**	**8**	**5.61**	**1.4**	**2**	**3.96**	**0.5**	**6**	**5.12**	**1.2**	**17**	**17.32**	**1.0**
Buccal cavity, pharynx	**0**	**0.04**	**0.0**	**0**	**0.08**	**0.0**	**0**	**0.05**	**0.0**	**0**	**0.07**	**0.0**	**0**	**0.23**	**0.0**
Lip	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Tongue	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Gum, other mouth	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Pharynx	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Digestive system	**1**	**0.94**	**1.1**	**3**	**1.95**	**1.5**	**2**	**1.38**	**1.4**	**1**	**1.80**	**0.6**	**7**	**6.06**	**1.2**
Esophagus	0	0.03	0.0	0	0.05	0.0	0	0.04	0.0	0	0.05	0.0	0	0.17	0.0
Stomach	0	0.26	0.0	1	0.47	2.1	1	0.32	3.1	0	0.38	0.0	2	1.43	1.4
Colon	0	0.28	0.0	1	0.63	1.6	0	0.45	0.0	0	0.61	0.0	1	1.98	0.5
Rectum	0	0.16	0.0	0	0.34	0.0	0	0.24	0.0	0	0.31	0.0	0	1.05	0.0
Liver, biliary	0	0.08	0.0	0	0.18	0.0	0	0.13	0.0	0	0.18	0.0	0	0.56	0.0
Pancreas	1	0.09	11.2	1	0.21	4.8	1	0.15	6.8	1	0.21	4.8	4	0.66	6.1[b]
Respiratory system	**0**	**0.13**	**0.0**	**1**	**0.29**	**3.4**	**0**	**0.21**	**0.0**	**0**	**0.30**	**0.0**	**1**	**0.93**	**1.1**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Larynx	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Trachea, bronchus, lung	0	0.11	0.0	0	0.25	0.0	0	0.18	0.0	0	0.26	0.0	0	0.79	0.0
Female breast	0	0.54	0.0	3	1.17	2.6	0	0.82	0.0	3	1.04	2.9	6	3.57	1.7
Female genital tract	**0**	**0.49**	**0.0**	**1**	**1.05**	**1.0**	**0**	**0.72**	**0.0**	**1**	**0.89**	**1.1**	**2**	**3.14**	**0.6**
Cervix uteri	0	0.16	0.0	0	0.34	0.0	0	0.22	0.0	0	0.25	0.0	0	0.97	0.0
Corpus uteri	0	0.14	0.0	0	0.30	0.0	0	0.21	0.0	0	0.27	0.0	0	0.92	0.0
Uterus, NOS	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Ovary, fallopian tubes	0	0.15	0.0	1	0.31	3.2	0	0.22	0.0	1	0.28	3.5	2	0.96	2.1
Kidney, renal pelvis, ureter	0	0.07	0.0	0	0.15	0.0	0	0.11	0.0	0	0.14	0.0	0	0.47	0.0
Bladder, other urinary	0	0.07	0.0	0	0.16	0.0	0	0.12	0.0	0	0.16	0.0	0	0.51	0.0
Melanoma of the skin	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	1	0.07	13.6	1	0.23	4.3
Eye	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Brain, central nervous system	0	0.05	0.0	0	0.11	0.0	0	0.07	0.0	0	0.10	0.0	0	0.33	0.0
Thyroid gland	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Connective tissue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Lymphatic, hematopoietic system	**0**	**0.14**	**0.0**	**0**	**0.30**	**0.0**	**0**	**0.22**	**0.0**	**0**	**0.30**	**0.0**	**0**	**0.96**	**0.0**
Non-Hodgkin's lymphoma	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.09	0.0	0	0.29	0.0
Hodgkin's disease	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.07	0.0
Multiple myeloma	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.06	0.0	0	0.19	0.0
Leukemias	0	0.06	0.0	0	0.13	0.0	0	0.09	0.0	0	0.12	0.0	0	0.40	0.0
Chronic lymphocytic	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.18	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.12	0.0

[a] ICD-7 code = 160.

[b] $P < .05$.

LARYNX
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the larynx, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	3,344	503	3,847
No. who developed a second primary cancer	321	47	368
Average age at diagnosis of first cancer, yr	63	61	63
Average yr of diagnosis of first cancer	1967	1968	1967
Person-yr of follow-up	19,754	3,215	22,969
Average follow-up, yr	5.9	6.4	6.0
Percent given radiotherapy for first cancer	90	90	90

[a] ICD-7 code = 161.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the larynx in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	310	84.2
Only the first cancer	33	9.0
Only the second cancer	20	5.4
Neither first nor second cancer	5	1.4
Total second primary cancers	368	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LARYNX
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the larynx among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,847			3,104			1,598			805			3,847		
Person-yr in interval	3,511			8,611			5,819			5,029			22,969		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**32**	**36.37**	**0.9**	**128**	**95.11**	**1.3**[b]	**96**	**71.69**	**1.3**[b]	**112**	**79.30**	**1.4**[b]	**368**	**282.46**	**1.3**[b]
All excluding site of initial cancer	**31**	**35.85**	**0.9**	**128**	**93.77**	**1.4**[b]	**96**	**70.70**	**1.4**[b]	**112**	**78.34**	**1.4**[b]	**367**	**278.65**	**1.3**[b]
Buccal cavity, pharynx	**1**	**1.12**	**0.9**	**3**	**2.84**	**1.1**	**3**	**2.07**	**1.4**	**9**	**2.06**	**4.4**[b]	**16**	**8.08**	**2.0**[b]
Lip	1	0.59	1.7	2	1.48	1.4	2	1.06	1.9	3	1.06	2.8	8	4.18	1.9
Tongue	0	0.09	0.0	1	0.22	4.5	0	0.17	0.0	0	0.16	0.0	1	0.63	1.6
Salivary gland	0	0.10	0.0	0	0.25	0.0	1	0.18	5.6	0	0.18	0.0	1	0.70	1.4
Gum, other mouth	0	0.16	0.0	0	0.43	0.0	0	0.32	0.0	3	0.35	8.6[b]	3	1.26	2.4
Pharynx	0	0.18	0.0	0	0.47	0.0	0	0.34	0.0	3	0.33	9.1[b]	3	1.31	2.3
Digestive system	**12**	**12.83**	**0.9**	**40**	**33.27**	**1.2**	**24**	**25.09**	**1.0**	**26**	**28.32**	**0.9**	**102**	**99.52**	**1.0**
Esophagus	0	0.55	0.0	1	1.41	0.7	0	1.03	0.0	0	1.10	0.0	1	4.09	0.2
Stomach	5	3.76	1.3	12	9.53	1.3	5	7.06	0.7	8	7.65	1.0	30	27.99	1.1
Colon	2	3.07	0.7	9	8.12	1.1	8	6.22	1.3	5	7.46	0.7	24	24.87	1.0
Rectum	0	2.85	0.0	7	7.38	0.9	3	5.55	0.5	5	6.09	0.8	15	21.85	0.7
Liver, biliary	3	0.77	3.9	2	2.07	1.0	1	1.60	0.6	2	1.94	1.0	8	6.38	1.3
Pancreas	1	1.41	0.7	6	3.74	1.6	7	2.86	2.4	5	3.28	1.5	19	11.28	1.7[b]
Respiratory system	**9**	**7.57**	**1.2**	**45**	**19.85**	**2.3**[b]	**41**	**14.89**	**2.8**[b]	**39**	**15.30**	**2.5**[b]	**134**	**57.60**	**2.3**[b]
Nasal cavities, sinuses	0	0.10	0.0	0	0.25	0.0	0	0.19	0.0	0	0.19	0.0	0	0.73	0.0
Larynx	1	0.52	1.9	0	1.34	0.0	0	0.99	0.0	0	0.96	0.0	1	3.81	0.3
Trachea, bronchus, lung	8	6.64	1.2	45	17.45	2.6[b]	40	13.11	3.1[b]	38	13.46	2.8[b]	131	50.67	2.6[b]
Female breast	0	0.82	0.0	3	2.10	1.4	3	1.54	2.0	5	1.77	2.8	11	6.23	1.8
Female genital tract	**0**	**0.76**	**0.0**	**5**	**1.95**	**2.6**	**1**	**1.40**	**0.7**	**1**	**1.46**	**0.7**	**7**	**5.57**	**1.3**
Cervix uteri	0	0.25	0.0	4	0.62	6.5[b]	0	0.41	0.0	1	0.39	2.6	5	1.68	3.0
Corpus uteri	0	0.23	0.0	0	0.59	0.0	0	0.44	0.0	0	0.45	0.0	0	1.71	0.0
Uterus, NOS	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Ovary, fallopian tubes	0	0.23	0.0	1	0.58	1.7	1	0.43	2.3	0	0.47	0.0	2	1.71	1.2
Prostate gland	3	4.09	0.7	8	11.09	0.7	10	8.78	1.1	10	10.92	0.9	31	34.88	0.9
Testis	0	0.13	0.0	0	0.30	0.0	0	0.19	0.0	0	0.16	0.0	0	0.78	0.0
Kidney, renal pelvis, ureter	0	1.20	0.0	2	3.15	0.6	0	2.36	0.0	3	2.59	1.2	5	9.31	0.5
Bladder, other urinary	2	2.89	0.7	7	7.68	0.9	8	5.84	1.4	14	6.49	2.2[b]	31	22.91	1.4
Melanoma of the skin	0	0.36	0.0	0	0.92	0.0	0	0.67	0.0	1	0.66	1.5	1	2.60	0.4
Eye	0	0.11	0.0	0	0.29	0.0	0	0.21	0.0	0	0.21	0.0	0	0.83	0.0
Brain, central nervous system	0	0.70	0.0	4	1.76	2.3	1	1.24	0.8	1	1.10	0.9	6	4.79	1.3
Thyroid gland	2	0.12	16.7[b]	0	0.31	0.0	0	0.23	0.0	0	0.25	0.0	2	0.92	2.2
Bone	0	0.07	0.0	0	0.16	0.0	0	0.12	0.0	0	0.12	0.0	0	0.47	0.0
Connective tissue	0	0.12	0.0	0	0.31	0.0	1	0.22	4.5	0	0.23	0.0	1	0.87	1.1
Lymphatic, hematopoietic system	**3**	**2.32**	**1.3**	**11**	**6.10**	**1.8**	**3**	**4.59**	**0.7**	**2**	**5.10**	**0.4**	**19**	**18.11**	**1.0**
Non-Hodgkin's lymphoma	1	0.63	1.6	6	1.63	3.7[b]	1	1.23	0.8	1	1.33	0.8	9	4.82	1.9
Hodgkin's disease	0	0.17	0.0	0	0.44	0.0	0	0.31	0.0	0	0.30	0.0	0	1.22	0.0
Multiple myeloma	0	0.44	0.0	3	1.15	2.6	0	0.88	0.0	0	1.00	0.0	3	3.46	0.9
Leukemias	2	1.06	1.9	2	2.80	0.7	2	2.12	0.9	1	2.43	0.4	7	8.42	0.8
Chronic lymphocytic	1	0.56	1.8	1	1.50	0.7	1	1.15	0.9	0	1.34	0.0	3	4.55	0.7
Acute nonlymphocytic	1	0.28	3.6	0	0.73	0.0	1	0.56	1.8	1	0.64	1.6	3	2.19	1.4

[a] ICD-7 code = 161.
[b] $P < .05$.

LARYNX
MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the larynx among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,344			2,693			1,383			692			3,344		
Person-yr in interval	3,049			7,457			5,019			4,230			19,754		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**28**	**32.60**	**0.9**	**111**	**85.40**	**1.3^b**	**86**	**64.38**	**1.3^b**	**96**	**70.41**	**1.4^b**	**321**	**252.78**	**1.3^b**
All excluding site of initial cancer	**27**	**32.09**	**0.8**	**111**	**84.08**	**1.3^b**	**86**	**63.41**	**1.4^b**	**96**	**69.47**	**1.4^b**	**320**	**249.04**	**1.3^b**
Buccal cavity, pharynx	**1**	**1.07**	**0.9**	**3**	**2.71**	**1.1**	**3**	**1.97**	**1.5**	**8**	**1.94**	**4.1^b**	**15**	**7.68**	**2.0^b**
Lip	1	0.58	1.7	2	1.46	1.4	2	1.05	1.9	3	1.04	2.9	8	4.12	1.9
Tongue	0	0.08	0.0	1	0.20	5.1	0	0.15	0.0	0	0.14	0.0	1	0.56	1.8
Salivary gland	0	0.09	0.0	0	0.22	0.0	1	0.16	6.3	0	0.16	0.0	1	0.62	1.6
Gum, other mouth	0	0.15	0.0	0	0.39	0.0	0	0.29	0.0	2	0.31	6.6	2	1.14	1.8
Pharynx	0	0.17	0.0	0	0.44	0.0	0	0.32	0.0	3	0.31	9.8^b	3	1.24	2.4
Digestive system	**11**	**11.62**	**0.9**	**37**	**30.16**	**1.2**	**23**	**22.66**	**1.0**	**22**	**25.09**	**0.9**	**93**	**89.54**	**1.0**
Esophagus	0	0.52	0.0	1	1.32	0.8	0	0.96	0.0	0	1.01	0.0	1	3.81	0.3
Stomach	4	3.46	1.2	11	8.79	1.3	5	6.50	0.8	7	6.95	1.0	27	25.70	1.1
Colon	2	2.69	0.7	8	7.12	1.1	8	5.43	1.5	5	6.37	0.8	23	21.61	1.1
Rectum	0	2.63	0.0	6	6.81	0.9	3	5.11	0.6	4	5.54	0.7	13	20.08	0.6
Liver, biliary	3	0.67	4.4	2	1.80	1.1	1	1.38	0.7	1	1.62	0.6	7	5.47	1.3
Pancreas	1	1.29	0.8	6	3.41	1.8	6	2.60	2.3	5	2.91	1.7	18	10.20	1.8^b
Respiratory system	**9**	**7.36**	**1.2**	**40**	**19.30**	**2.1^b**	**36**	**14.46**	**2.5^b**	**37**	**14.78**	**2.5^b**	**122**	**55.90**	**2.2^b**
Nasal cavities, sinuses	0	0.09	0.0	0	0.24	0.0	0	0.18	0.0	0	0.18	0.0	0	0.68	0.0
Larynx	1	0.51	1.9	0	1.32	0.0	0	0.97	0.0	0	0.94	0.0	1	3.74	0.3
Trachea, bronchus, lung	8	6.46	1.2	40	16.98	2.4^b	35	12.74	2.7^b	36	13.02	2.8^b	119	49.20	2.4^b
Prostate gland	3	4.09	0.7	8	11.09	0.7	10	8.78	1.1	10	10.92	0.9	31	34.88	0.9
Testis	0	0.13	0.0	0	0.30	0.0	0	0.19	0.0	0	0.16	0.0	0	0.78	0.0
Kidney, renal pelvis, ureter	0	1.10	0.0	2	2.89	0.7	0	2.16	0.0	3	2.34	1.3	5	8.50	0.6
Bladder, other urinary	2	2.79	0.7	7	7.41	0.9	8	5.63	1.4	13	6.20	2.1^b	30	22.03	1.4
Melanoma of the skin	0	0.30	0.0	0	0.77	0.0	0	0.56	0.0	1	0.54	1.8	1	2.17	0.5
Eye	0	0.10	0.0	0	0.26	0.0	0	0.19	0.0	0	0.19	0.0	0	0.75	0.0
Brain, central nervous system	0	0.62	0.0	4	1.55	2.6	1	1.09	0.9	0	0.94	0.0	5	4.19	1.2
Thyroid gland	0	0.10	0.0	0	0.25	0.0	0	0.18	0.0	0	0.19	0.0	0	0.72	0.0
Bone	0	0.06	0.0	0	0.15	0.0	0	0.11	0.0	0	0.11	0.0	0	0.42	0.0
Connective tissue	0	0.11	0.0	0	0.28	0.0	1	0.20	5.0	0	0.20	0.0	1	0.78	1.3
Lymphatic, hematopoietic system	**2**	**2.13**	**0.9**	**10**	**5.59**	**1.8**	**3**	**4.20**	**0.7**	**1**	**4.58**	**0.2**	**16**	**16.50**	**1.0**
Non-Hodgkin's lymphoma	1	0.57	1.8	5	1.48	3.4^b	1	1.11	0.9	1	1.17	0.9	8	4.33	1.8
Hodgkin's disease	0	0.16	0.0	0	0.40	0.0	0	0.28	0.0	0	0.27	0.0	0	1.11	0.0
Multiple myeloma	0	0.40	0.0	3	1.05	2.8	0	0.80	0.0	0	0.89	0.0	3	3.14	1.0
Leukemias	1	0.98	1.0	2	2.59	0.8	2	1.96	1.0	0	2.21	0.0	5	7.75	0.6
Chronic lymphocytic	0	0.53	0.0	1	1.41	0.7	1	1.08	0.9	0	1.24	0.0	2	4.26	0.5
Acute nonlymphocytic	1	0.25	4.1	0	0.66	0.0	1	0.51	2.0	0	0.57	0.0	2	1.98	1.0

[a] ICD-7 code = 161.
[b] $P < .05$.

LARYNX
FEMALES

TABLE 2E *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the larynx among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	503			411			215			113			503		
Person-yr in interval	462			1,155			800			798			3,215		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**3.77**	**1.1**	**17**	**9.71**	**1.8**[b]	**10**	**7.31**	**1.4**	**16**	**8.89**	**1.8**[b]	**47**	**29.68**	**1.6**[b]
All excluding site of initial cancer	**4**	**3.76**	**1.1**	**17**	**9.69**	**1.8**[b]	**10**	**7.29**	**1.4**	**16**	**8.87**	**1.8**[b]	**47**	**29.61**	**1.6**[b]
Buccal cavity, pharynx	**0**	**0.05**	**0.0**	**0**	**0.13**	**0.0**	**0**	**0.10**	**0.0**	**1**	**0.12**	**8.2**	**1**	**0.40**	**2.5**
Lip	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Tongue	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Salivary gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Gum, other mouth	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	1	0.04	24.4	1	0.12	8.2
Pharynx	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Digestive system	**1**	**1.21**	**0.8**	**3**	**3.11**	**1.0**	**1**	**2.43**	**0.4**	**4**	**3.23**	**1.2**	**9**	**9.98**	**0.9**
Esophagus	0	0.03	0.0	0	0.09	0.0	0	0.07	0.0	0	0.09	0.0	0	0.28	0.0
Stomach	1	0.30	3.4	1	0.74	1.4	0	0.56	0.0	1	0.70	1.4	3	2.29	1.3
Colon	0	0.38	0.0	1	1.00	1.0	0	0.79	0.0	0	1.09	0.0	1	3.26	0.3
Rectum	0	0.22	0.0	1	0.57	1.8	0	0.44	0.0	1	0.55	1.8	2	1.77	1.1
Liver, biliary	0	0.10	0.0	0	0.27	0.0	0	0.22	0.0	1	0.32	3.1	1	0.91	1.1
Pancreas	0	0.12	0.0	0	0.33	0.0	1	0.26	3.9	0	0.37	0.0	1	1.08	0.9
Respiratory system	**0**	**0.21**	**0.0**	**5**	**0.55**	**9.1**[b]	**5**	**0.43**	**11.7**[b]	**2**	**0.52**	**3.9**	**12**	**1.70**	**7.0**[b]
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Larynx	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Trachea, bronchus, lung	0	0.18	0.0	5	0.47	10.6[b]	5	0.37	13.6[b]	2	0.44	4.5	12	1.47	8.2[b]
Female breast	0	0.82	0.0	3	2.10	1.4	3	1.54	2.0	5	1.77	2.8	11	6.23	1.8
Female genital tract	**0**	**0.76**	**0.0**	**5**	**1.95**	**2.6**	**1**	**1.40**	**0.7**	**1**	**1.46**	**0.7**	**7**	**5.57**	**1.3**
Cervix uteri	0	0.25	0.0	4	0.62	6.5[b]	0	0.41	0.0	1	0.39	2.6	5	1.68	3.0
Corpus uteri	0	0.23	0.0	0	0.59	0.0	0	0.44	0.0	0	0.45	0.0	0	1.71	0.0
Uterus, NOS	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Ovary, fallopian tubes	0	0.23	0.0	1	0.58	1.7	1	0.43	2.3	0	0.47	0.0	2	1.71	1.2
Kidney, renal pelvis, ureter	0	0.10	0.0	0	0.26	0.0	0	0.20	0.0	0	0.25	0.0	0	0.81	0.0
Bladder, other urinary	0	0.10	0.0	0	0.27	0.0	0	0.21	0.0	1	0.29	3.4	1	0.88	1.1
Melanoma of the skin	0	0.06	0.0	0	0.15	0.0	0	0.11	0.0	0	0.12	0.0	0	0.43	0.0
Eye	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Brain, central nervous system	0	0.08	0.0	0	0.21	0.0	0	0.15	0.0	1	0.16	6.4	1	0.60	1.7
Thyroid gland	2	0.02	81.0[b]	0	0.06	0.0	0	0.05	0.0	0	0.06	0.0	2	0.20	9.8[b]
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Lymphatic, hematopoietic system	**1**	**0.19**	**5.2**	**1**	**0.51**	**2.0**	**0**	**0.39**	**0.0**	**1**	**0.52**	**1.9**	**3**	**1.61**	**1.9**
Non-Hodgkin's lymphoma	0	0.06	0.0	1	0.15	6.5	0	0.12	0.0	0	0.16	0.0	1	0.49	2.0
Hodgkin's disease	0	0.01	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.11	0.0
Multiple myeloma	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	0	0.11	0.0	0	0.32	0.0
Leukemias	1	0.08	12.5	0	0.21	0.0	0	0.16	0.0	1	0.22	4.6	2	0.67	3.0
Chronic lymphocytic	1	0.03	29.7	0	0.09	0.0	0	0.07	0.0	0	0.10	0.0	1	0.29	3.4
Acute nonlymphocytic	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	1	0.07	14.2	1	0.21	4.7

[a] ICD-7 code = 161.
[b] $P < .05$.

LUNG
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the trachea, bronchus, or lung, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	25,338	5,709	31,047
No. who developed a second primary cancer	400	95	495
Average age at diagnosis of first cancer, yr	64	63	64
Average yr of diagnosis of first cancer	1968	1969	1968
Person-yr of follow-up	37,597	7,896	45,493
Average follow-up, yr	1.5	1.4	1.5
Percent given radiotherapy for first cancer	24	23	24

[a] ICD-7 code = 162.0, 162.1.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the trachea, bronchus, or lung in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	415	83.8
Only the first cancer	38	7.7
Only the second cancer	30	6.1
Neither first nor second cancer	12	2.4
Total second primary cancers	495	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LUNG
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the trachea, bronchus, or lung among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	31,047			9,208			2,162			917			31,047		
Person-yr in interval	18,078			15,395			7,224			4,796			45,494		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**148**	**190.08**	**0.8**[b]	**178**	**160.90**	**1.1**	**82**	**86.45**	**0.9**	**87**	**71.42**	**1.2**	**495**	**508.85**	**1.0**
All excluding site of initial cancer	**146**	**153.88**	**0.9**	**170**	**128.67**	**1.3**[b]	**79**	**69.12**	**1.1**	**86**	**58.00**	**1.5**[b]	**481**	**409.67**	**1.2**[b]
Buccal cavity, pharynx	**2**	**5.59**	**0.4**	**7**	**4.73**	**1.5**	**3**	**2.44**	**1.2**	**4**	**1.87**	**2.1**	**16**	**14.63**	**1.1**
Lip	2	2.87	0.7	2	2.42	0.8	1	1.25	0.8	0	0.95	0.0	5	7.49	0.7
Tongue	0	0.44	0.0	0	0.37	0.0	0	0.18	0.0	2	0.14	14.3[b]	2	1.13	1.8
Salivary gland	0	0.50	0.0	1	0.42	2.4	0	0.22	0.0	1	0.16	6.3	2	1.29	1.6
Gum, other mouth	0	0.84	0.0	3	0.72	4.2	0	0.38	0.0	1	0.32	3.1	4	2.28	1.8
Pharynx	0	0.93	0.0	1	0.80	1.3	2	0.41	4.9	0	0.30	0.0	3	2.44	1.2
Digestive system	**67**	**64.16**	**1.0**	**48**	**52.68**	**0.9**	**25**	**28.43**	**0.9**	**33**	**24.25**	**1.4**	**173**	**169.51**	**1.0**
Esophagus	5	2.65	1.9	2	2.17	0.9	0	1.15	0.0	2	0.94	2.1	9	6.90	1.3
Stomach	12	17.61	0.7	14	13.93	1.0	6	7.35	0.8	5	6.20	0.8	37	45.09	0.8
Colon	12	15.86	0.8	13	13.13	1.0	4	7.23	0.6	11	6.43	1.7	40	42.65	0.9
Rectum	10	14.28	0.7	7	11.83	0.6	3	6.34	0.5	6	5.29	1.1	26	37.73	0.7
Liver, biliary	8	4.24	1.9	4	3.59	1.1	5	1.99	2.5	5	1.73	2.9	22	11.57	1.9[b]
Pancreas	16	7.51	2.1[b]	4	6.39	0.6	5	3.50	1.4	3	2.95	1.0	28	20.37	1.4
Respiratory system	**7**	**41.00**	**0.2**[b]	**21**	**36.41**	**0.6**[b]	**9**	**19.56**	**0.5**[b]	**3**	**15.13**	**0.2**[b]	**40**	**112.09**	**0.4**[b]
Nasal cavities, sinuses	1	0.50	2.0	0	0.42	0.0	0	0.23	0.0	0	0.17	0.0	1	1.33	0.8
Larynx	3	2.73	1.1	12	2.42	5.0[b]	6	1.27	4.7[b]	2	0.95	2.1	23	7.37	3.1[b]
Trachea, bronchus, lung	2	36.20	0.1[b]	8	32.23	0.2[b]	3	17.33	0.2[b]	1	13.42	0.1[b]	14	99.18	0.1[b]
Female breast	5	5.98	0.8	6	4.92	1.2	4	2.34	1.7	5	1.78	2.8	20	15.02	1.3
Female genital tract	**2**	**5.47**	**0.4**	**9**	**4.59**	**2.0**	**4**	**2.11**	**1.9**	**8**	**1.48**	**5.4**[b]	**23**	**13.66**	**1.7**[b]
Cervix uteri	0	1.72	0.0	3	1.46	2.1	2	0.63	3.1	2	0.40	5.1	7	4.21	1.7
Corpus uteri	0	1.67	0.0	2	1.42	1.4	0	0.67	0.0	6	0.47	12.7[b]	8	4.23	1.9
Uterus, NOS	0	0.09	0.0	2	0.07	29.3[b]	1	0.03	30.8	0	0.03	0.0	3	0.22	13.4[b]
Ovary, fallopian tubes	2	1.66	1.2	2	1.39	1.4	1	0.65	1.5	0	0.47	0.0	5	4.18	1.2
Prostate gland	16	19.80	0.8	17	16.33	1.0	3	9.59	0.3[b]	12	9.10	1.3	48	54.82	0.9
Testis	0	0.59	0.0	0	0.50	0.0	2	0.23	8.8	1	0.15	6.8	3	1.46	2.0
Kidney, renal pelvis, ureter	16	6.35	2.5[b]	18	5.47	3.3[b]	6	2.92	2.1	6	2.37	2.5	46	17.11	2.7[b]
Bladder, other urinary	12	15.18	0.8	27	13.21	2.0[b]	14	7.28	1.9[b]	13	6.03	2.2[b]	66	41.69	1.6[b]
Melanoma of the skin	1	1.93	0.5	2	1.68	1.2	0	0.84	0.0	0	0.62	0.0	3	5.08	0.6
Eye	0	0.60	0.0	0	0.51	0.0	0	0.26	0.0	0	0.19	0.0	0	1.57	0.0
Brain, central nervous system	2	3.80	0.5	2	3.35	0.6	1	1.64	0.6	0	1.12	0.0	5	9.89	0.5
Thyroid gland	1	0.67	1.5	0	0.56	0.0	0	0.29	0.0	0	0.23	0.0	1	1.77	0.6
Bone	0	0.32	0.0	0	0.27	0.0	0	0.14	0.0	0	0.10	0.0	0	0.83	0.0
Connective tissue	1	0.62	1.6	2	0.52	3.8	1	0.26	3.8	0	0.19	0.0	4	1.59	2.5
Lymphatic, hematopoietic system	**11**	**12.21**	**0.9**	**15**	**10.38**	**1.4**	**7**	**5.56**	**1.3**	**1**	**4.58**	**0.2**	**34**	**32.73**	**1.0**
Non-Hodgkin's lymphoma	4	3.35	1.2	3	2.86	1.0	3	1.52	2.0	0	1.23	0.0	10	8.96	1.1
Hodgkin's disease	1	0.90	1.1	1	0.78	1.3	0	0.38	0.0	0	0.27	0.0	2	2.34	0.9
Multiple myeloma	1	2.34	0.4	3	2.01	1.5	0	1.09	0.0	0	0.89	0.0	4	6.34	0.6
Leukemias	5	5.49	0.9	8	4.61	1.7	4	2.50	1.6	1	2.13	0.5	18	14.74	1.2
Chronic lymphocytic	3	2.88	1.0	6	2.41	2.5	2	1.32	1.5	1	1.14	0.9	12	7.76	1.5
Acute nonlymphocytic	1	1.48	0.7	2	1.28	1.6	1	0.70	1.4	0	0.59	0.0	4	4.04	1.0

[a] ICD-7 code = 162.0, 162.1.

[b] $P < .05$.

LUNG
MALES

TABLE 3D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the trachea, bronchus, or lung among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	25,338			7,644			1,786			769			25,338		
Person-yr in interval	14,862			12,707			6,025			4,003			37,597		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**121**	**162.73**	**0.7**[b]	**143**	**138.76**	**1.0**	**66**	**75.66**	**0.9**	**70**	**62.67**	**1.1**	**400**	**439.82**	**0.9**
All excluding site of initial cancer	**119**	**127.94**	**0.9**	**136**	**107.72**	**1.3**[b]	**63**	**58.91**	**1.1**	**69**	**49.71**	**1.4**[b]	**387**	**344.28**	**1.1**[b]
Buccal cavity, pharynx	**1**	**5.23**	**0.2**	**6**	**4.45**	**1.3**	**3**	**2.30**	**1.3**	**2**	**1.75**	**1.1**	**12**	**13.73**	**0.9**
Lip	1	2.82	0.4	2	2.38	0.8	1	1.23	0.8	0	0.93	0.0	4	7.36	0.5
Tongue	0	0.38	0.0	0	0.32	0.0	0	0.16	0.0	1	0.12	8.1	1	0.98	1.0
Salivary gland	0	0.43	0.0	1	0.36	2.8	0	0.19	0.0	1	0.14	7.1	2	1.12	1.8
Gum, other mouth	0	0.74	0.0	3	0.64	4.7	0	0.34	0.0	0	0.28	0.0	3	2.01	1.5
Pharynx	0	0.86	0.0	0	0.74	0.0	2	0.38	5.3	0	0.28	0.0	2	2.27	0.9
Digestive system	**54**	**55.55**	**1.0**	**38**	**46.00**	**0.8**	**21**	**25.03**	**0.8**	**33**	**21.18**	**1.6**[b]	**146**	**147.75**	**1.0**
Esophagus	4	2.42	1.7	2	2.00	1.0	0	1.06	0.0	2	0.85	2.3	8	6.33	1.3
Stomach	10	15.71	0.6	13	12.55	1.0	6	6.65	0.9	5	5.55	0.9	34	40.46	0.8
Colon	9	13.03	0.7	8	10.89	0.7	4	6.08	0.7	11	5.39	2.0[b]	32	35.39	0.9
Rectum	9	12.71	0.7	6	10.58	0.6	3	5.72	0.5	6	4.75	1.3	24	33.76	0.7
Liver, biliary	6	3.45	1.7	3	2.97	1.0	5	1.67	3.0	5	1.43	3.5[b]	19	9.53	2.0[b]
Pancreas	13	6.55	2.0[b]	3	5.63	0.5	2	3.11	0.6	3	2.60	1.2	21	17.90	1.2
Respiratory system	**7**	**39.37**	**0.2**[b]	**20**	**35.04**	**0.6**[b]	**9**	**18.89**	**0.5**[b]	**3**	**14.60**	**0.2**[b]	**39**	**107.89**	**0.4**[b]
Nasal cavities, sinuses	1	0.46	2.2	0	0.39	0.0	0	0.21	0.0	0	0.16	0.0	1	1.22	0.8
Larynx	3	2.66	1.1	12	2.36	5.1[b]	6	1.24	4.8[b]	2	0.93	2.2	23	7.19	3.2[b]
Trachea, bronchus, lung	2	34.79	0.1[b]	7	31.04	0.2[b]	3	16.75	0.2[b]	1	12.96	0.1[b]	13	95.54	0.1[b]
Prostate gland	16	19.80	0.8	17	16.33	1.0	3	9.59	0.3[b]	12	9.10	1.3	48	54.82	0.9
Testis	0	0.59	0.0	0	0.50	0.0	2	0.23	8.8	1	0.15	6.8	3	1.46	2.0
Kidney, renal pelvis, ureter	13	5.60	2.3[b]	16	4.85	3.3[b]	6	2.62	2.3	6	2.12	2.8[b]	41	15.19	2.7[b]
Bladder, other urinary	12	14.39	0.8	26	12.57	2.1[b]	13	6.95	1.9	12	5.75	2.1[b]	63	39.66	1.6[b]
Melanoma of the skin	1	1.50	0.7	1	1.31	0.8	0	0.67	0.0	0	0.50	0.0	2	3.98	0.5
Eye	0	0.52	0.0	0	0.45	0.0	0	0.23	0.0	0	0.17	0.0	0	1.38	0.0
Brain, central nervous system	2	3.21	0.6	1	2.84	0.4	1	1.40	0.7	0	0.95	0.0	4	8.39	0.5
Thyroid gland	1	0.49	2.1	0	0.42	0.0	0	0.22	0.0	0	0.17	0.0	1	1.31	0.8
Bone	0	0.28	0.0	0	0.24	0.0	0	0.12	0.0	0	0.09	0.0	0	0.73	0.0
Connective tissue	1	0.53	1.9	2	0.45	4.5	0	0.23	0.0	0	0.17	0.0	3	1.38	2.2
Lymphatic, hematopoietic system	**8**	**10.75**	**0.7**	**14**	**9.20**	**1.5**	**6**	**4.97**	**1.2**	**1**	**4.08**	**0.2**	**29**	**29.00**	**1.0**
Non-Hodgkin's lymphoma	2	2.90	0.7	3	2.50	1.2	2	1.34	1.5	0	1.07	0.0	7	7.81	0.9
Hodgkin's disease	1	0.80	1.2	1	0.69	1.4	0	0.34	0.0	0	0.24	0.0	2	2.08	1.0
Multiple myeloma	1	2.05	0.5	3	1.77	1.7	0	0.97	0.0	0	0.79	0.0	4	5.58	0.7
Leukemias	4	4.89	0.8	7	4.13	1.7	4	2.26	1.8	1	1.92	0.5	16	13.21	1.2
Chronic lymphocytic	3	2.63	1.1	5	2.21	2.3	2	1.22	1.6	1	1.05	0.9	11	7.12	1.5
Acute nonlymphocytic	0	1.28	0.0	2	1.11	1.8	1	0.62	1.6	0	0.52	0.0	3	3.53	0.8

[a] ICD-7 code = 162.0, 162.1.

[b] $P < .05$.

LUNG
FEMALES

TABLE 3E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the trachea, bronchus, or lung among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,709			1,564			376			148			5,709		
Person-yr in interval	3,216			2,688			1,199			792			7,896		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**27**	**27.35**	**1.0**	**35**	**22.14**	**1.6**[b]	**16**	**10.79**	**1.5**	**17**	**8.75**	**1.9**[b]	**95**	**69.03**	**1.4**[b]
All excluding site of initial cancer	**27**	**25.94**	**1.0**	**34**	**20.95**	**1.6**[b]	**16**	**10.21**	**1.6**	**17**	**8.29**	**2.1**[b]	**94**	**65.39**	**1.4**[b]
Buccal cavity, pharynx	**1**	**0.36**	**2.8**	**1**	**0.28**	**3.5**	**0**	**0.14**	**0.0**	**2**	**0.12**	**16.9**[b]	**4**	**0.90**	**4.5**[b]
Lip	1	0.05	18.9	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	1	0.13	7.6
Tongue	0	0.06	0.0	0	0.05	0.0	0	0.02	0.0	1	0.02	48.2	1	0.15	6.7
Salivary gland	0	0.07	0.0	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	0	0.17	0.0
Gum, other mouth	0	0.10	0.0	0	0.08	0.0	0	0.04	0.0	1	0.04	25.4	1	0.27	3.8
Pharynx	0	0.07	0.0	1	0.06	17.9	0	0.03	0.0	0	0.02	0.0	1	0.17	5.8
Digestive system	**13**	**8.61**	**1.5**	**10**	**6.68**	**1.5**	**4**	**3.40**	**1.2**	**0**	**3.07**	**0.0**	**27**	**21.76**	**1.2**
Esophagus	1	0.23	4.4	0	0.17	0.0	0	0.09	0.0	0	0.09	0.0	1	0.57	1.8
Stomach	2	1.90	1.1	1	1.38	0.7	0	0.70	0.0	0	0.65	0.0	3	4.63	0.6
Colon	3	2.83	1.1	5	2.24	2.2	0	1.15	0.0	0	1.04	0.0	8	7.26	1.1
Rectum	1	1.57	0.6	1	1.25	0.8	0	0.62	0.0	0	0.54	0.0	2	3.97	0.5
Liver, biliary	2	0.79	2.5	1	0.62	1.6	0	0.32	0.0	0	0.30	0.0	3	2.04	1.5
Pancreas	3	0.96	3.1	1	0.76	1.3	3	0.39	7.6[b]	0	0.35	0.0	7	2.47	2.8[b]
Respiratory system	**0**	**1.63**	**0.0**	**1**	**1.37**	**0.7**	**0**	**0.67**	**0.0**	**0**	**0.53**	**0.0**	**1**	**4.20**	**0.2**
Nasal cavities, sinuses	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.11	0.0
Larynx	0	0.07	0.0	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	0	0.18	0.0
Trachea, bronchus, lung	0	1.41	0.0	1	1.19	0.8	0	0.58	0.0	0	0.46	0.0	1	3.64	0.3
Female breast	5	5.98	0.8	6	4.92	1.2	4	2.34	1.7	5	1.78	2.8	20	15.02	1.3
Female genital tract	**2**	**5.47**	**0.4**	**9**	**4.59**	**2.0**	**4**	**2.11**	**1.9**	**8**	**1.48**	**5.4**[b]	**23**	**13.66**	**1.7**[b]
Cervix uteri	0	1.72	0.0	3	1.46	2.1	2	0.63	3.1	2	0.40	5.1	7	4.21	1.7
Corpus uteri	0	1.67	0.0	2	1.42	1.4	0	0.67	0.0	6	0.47	12.7[b]	8	4.23	1.9
Uterus, NOS	0	0.09	0.0	2	0.07	29.3[b]	1	0.03	30.8	0	0.03	0.0	3	0.22	13.4[b]
Ovary, fallopian tubes	2	1.66	1.2	2	1.39	1.4	1	0.65	1.5	0	0.47	0.0	5	4.18	1.2
Kidney, renal pelvis, ureter	3	0.75	4.0	2	0.62	3.2	0	0.30	0.0	0	0.25	0.0	5	1.92	2.6
Bladder, other urinary	0	0.79	0.0	1	0.64	1.6	1	0.33	3.1	1	0.28	3.6	3	2.03	1.5
Melanoma of the skin	0	0.43	0.0	1	0.37	2.7	0	0.17	0.0	0	0.12	0.0	1	1.10	0.9
Eye	0	0.08	0.0	0	0.06	0.0	0	0.03	0.0	0	0.02	0.0	0	0.19	0.0
Brain, central nervous system	0	0.59	0.0	1	0.51	2.0	0	0.24	0.0	0	0.17	0.0	1	1.50	0.7
Thyroid gland	0	0.18	0.0	0	0.14	0.0	0	0.07	0.0	0	0.06	0.0	0	0.46	0.0
Bone	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.10	0.0
Connective tissue	0	0.09	0.0	0	0.07	0.0	1	0.03	30.6	0	0.02	0.0	1	0.21	4.7
Lymphatic, hematopoietic system	**3**	**1.46**	**2.1**	**1**	**1.18**	**0.8**	**1**	**0.59**	**1.7**	**0**	**0.50**	**0.0**	**5**	**3.73**	**1.3**
Non-Hodgkin's lymphoma	2	0.45	4.5	0	0.36	0.0	1	0.18	5.5	0	0.16	0.0	3	1.15	2.6
Hodgkin's disease	0	0.10	0.0	0	0.09	0.0	0	0.04	0.0	0	0.03	0.0	0	0.26	0.0
Multiple myeloma	0	0.29	0.0	0	0.24	0.0	0	0.12	0.0	0	0.10	0.0	0	0.76	0.0
Leukemias	1	0.60	1.7	1	0.48	2.1	0	0.24	0.0	0	0.21	0.0	2	1.53	1.3
Chronic lymphocytic	0	0.25	0.0	1	0.20	5.1	0	0.10	0.0	0	0.09	0.0	1	0.64	1.6
Acute nonlymphocytic	1	0.20	5.0	0	0.17	0.0	0	0.08	0.0	0	0.07	0.0	1	0.51	1.9

[a] ICD-7 code = 162.0, 162.1.

[b] $P < .05$.

Second Cancer Following Cancer of the Female Breast in Denmark, 1943–80 [1]

Marianne Ewertz [2] *and* Henning T. Mouridsen [3]

ABSTRACT—The risk of a person developing a second primary cancer was evaluated in approximately 55,000 women diagnosed with breast cancer in Denmark between 1943 and 1980. Excluding second cancers of the contralateral breast, 2,480 new cancers were observed compared with 2,398 expected (relative risk = 1.03; 95% CI = 0.99–1.08). Breast cancer patients followed for 10 years or more showed a significant 13% excess of all second primary tumors. Significant excesses of cancers of the lung, bone, and connective tissue were observed. Although some misclassification of metastases may have occurred, the risk of second cancers at these sites (as well as the salivary gland and esophagus) increased significantly with time and was especially high among women followed for 10 years or more. These observations suggest that radiation, as a part of the initial treatment, may have been involved. Radiation or chemotherapy, or both, may also have influenced the risk of acute nonlymphocytic leukemia (51 cases observed vs. 20.7 expected), which remained significantly elevated after the first year of follow-up. Common risk factors, related to reproductive experience and nutrition, may have contributed to the excess risk of cancers of the ovary and colon. On the other hand, an anticipated excess of cancer of the corpus uteri was not found, although cancer of the uterus not otherwise specified was significantly increased. Significant deficits were observed for second cancers of the liver and biliary tract, due perhaps to underreporting or conservative coding practices, or both. A significant excess of malignant melanoma was not easily explained but might indicate a common hormonal etiology with breast cancer. Future studies should clarify the role of life-style factors and various treatment modalities on the risk of cancer development subsequent to breast cancer.—Natl Cancer Inst Monogr 68: 325–329, 1985.

Breast cancer is the most frequent cancer among females and accounts for 22% of all malignant disease in Danish women. The age-standardized incidence rate of breast cancer remained constant, approximately 44/100,000 woman-years between 1943 and 1960, but then it rose steadily to 63/100,000 woman-years in 1978–80 (*1, 2*). The lifetime risk (from birth to age 75) is about 7%. Breast cancer incidence rises rapidly until the age of 45–50 years, then levels off, and continues to increase at a slow rate after age 55. The characteristic "hook" in age-incidence curves seen around age 50 was first described by Clemmesen (*3*). Other demographic characteristics associated with elevated rates of breast cancer include urban residence, high socioeconomic status, and never being married (*1, 4*). Personal risk factors for breast cancer are related to reproduction (early age at menarche, late age at first full-term pregnancy, and late menopause), nutrition (diet and increased body weight in postmenopausal women), and a family history of breast cancer. Exogenous factors that increase the risk of breast cancer are exposure to ionizing radiation and possibly estrogens (*5*). Previous studies of multiple primaries after breast cancer have found increased risks of new cancers of the contralateral breast (*6*), colon (*6*), ovary (*6, 7*), uterus (*6, 7*), connective tissue (*6*), and thyroid (*8*), as well as melanoma (*6, 9*) and leukemia (*7, 10*).

Compared with other cancers, the prognosis after breast cancer is relatively favorable. Since 1943, the overall 5-year relative survival rate increased approximately 10%. The increase was most pronounced for cases diagnosed between 1943 and 1957, whereas only little improvement occurred thereafter. When all age groups and stages of disease were combined, the 5-year relative survival rate was 57% for cases diagnosed between 1963 and 1967 (*1*). Treatment for breast cancer in Denmark was standardized in 1977 when the Danish Breast Cancer Cooperative Group initiated a nationwide clinical trial. This randomized trial (*11*) includes about 90% of all new cases and introduced adjuvant therapy with cytotoxic drugs and tamoxifen to patients with an unfavorable prognosis (large tumors or spread to regional lymph nodes, or both). Preliminary results indicate that the recurrence rate is reduced by cytotoxic drugs in premenopausal women and by tamoxifen in postmenopausal women (*12*). Survival results are not yet available from these trials.

RESULTS

Between 1943 and 1980, of the 54,964 women who survived 2 or more months after a diagnosis of breast cancer in Denmark, the average age at diagnosis was 60 years and the average follow-up was 6.3 years. The initial treatment included surgery in 86% and radiation in 69% of the patients.

A total of 2,480 breast cancer patients (or 4.5%) developed a second tumor. In 80% of these, both the first and second cancers were histologically verified. On the basis of rates in the general population, 2,398 cancers were expected (RR = 1.03; 95% CI = 0.99–1.08). Second cancers in the contralateral breast are not included because only the first diagnosis of primary breast cancer was computerized by the Registry. Significantly increased risks

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ABBREVIATIONS: RR = relative risk(s); CI = confidence interval; NOS = not otherwise specified; ANLL = acute nonlymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, The Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Marianne Ewertz, M.D.

[3] Department of Oncology I, Finsen Institute, Strandboulevarden 49, DK-2100 Copenhagen, Denmark.

were found for leukemia, malignant melanoma, and cancers of the ovary, uterus NOS, lung, bone, and connective tissue. Nonsignificant elevations were seen for cancers of the lip, salivary gland, mouth, kidney, and thyroid. The risk of second cancers of the liver and biliary tract was significantly decreased. The risk of cervical cancer was also below expectation, though of borderline significance (RR = 0.9; 95% CI = 0.7–1.0).

Among 11,273 women who survived for 10 or more years, an excess of second tumors was apparent (RR = 1.13; 95% CI = 1.05–1.21). Significant excesses persisted over time for cancer of the lung, ovary, connective tissue, and ANLL. The overall elevation of risk of cancer in the salivary glands was due to an excess observed after 10 or more years (RR = 3.2; 95% CI = 1.3–6.5). The risk of second cancers of the esophagus and colon increased significantly with time ($P < .0001$ for trend), reaching RR of 1.7 (95% CI = 1.0–2.9) and 1.2 (95% CI = 1.0–1.4), respectively, after 10 years or more of survival. The risk of ANLL remained significantly elevated after the first year of observation. Of the female genital organs, the risk of a second cancer in the uterus NOS decreased significantly with time ($P = .02$ for trend), whereas the risk of developing a second ovarian cancer increased significantly ($P = .0004$ for trend).

DISCUSSION

Breast cancer patients surviving 5 or more years after initial diagnosis developed significantly more cancers than expected based on rates prevailing in the general population. Five years after the primary diagnosis, the excess was 10% and it increased to 13% after 10 or more years of follow-up. The excess second cancers were distributed over a wide range of sites.

The lung, bone, and connective tissue are common sites for metastases of breast cancer (*13*); a detailed review of the original notifications would be required to rule out a metastasic lesion. However, these 3 sites, as well as the salivary gland and esophagus, may have been exposed to radiation during the initial or subsequent course of treatment. The minimum latent period for radiation-induced solid tumors has been estimated to be about 10 years (*14*). The significant trends of increasing risks over time and the high RR among women followed 10 years or more after the first primary diagnosis (and initial treatment) indicate that radiation may be involved in the etiology of second cancers of the lungs, bone, connective tissue, salivary glands, and esophagus (*15*). However, a more in-depth evaluation of the location of the second tumor in relation to the radiation field is needed before any conclusions can be reached. The absence of an excess of thyroid cancer, a highly radiosensitive site, is noteworthy.

Since systemic breast cancer therapy with cytotoxic drugs was introduced in the mid-1970s in Denmark, the observation period is still too short for us to evaluate its influence on the risk of second solid tumors. Clinical trials of adjuvant chemotherapy for breast cancer (*16–19*) have not demonstrated any excess cancer risk associated with cytotoxic drugs after 4–10 years of follow-up. Risk of leukemias in relation to breast cancer treatment, however, has been studied by others (*7, 10, 20*). Curtis et al. (*10*) reported that radiation and chemotherapy were associated with fourfold and eightfold increased risks, respectively, of ANLL. In the present study, we also found that the excess risk of leukemia was limited to ANLL. Although we could not examine the different treatments separately, the twofold increased risk of leukemia is of the same magnitude as found by Curtis and associates (*10*) when all treatments, including surgery, were combined. This suggests an effect of breast cancer treatment that needs further study.

The elevated risks of cancers of the ovary and colon confirm what has been found previously and support the hypothesis of a common etiology (*5*). Contrary to expectation, the risk of cancer of the corpus uteri was not increased. However, if hysterectomies were performed more frequently among breast cancer patients than in the general female population, fewer women with intact uteri would be at risk and the expected number generated from population rates would be an overestimate. Results from a case–control study on this particular group of patients in Denmark indicate that an increased risk of cancer of the corpus uteri may be confined to a subgroup of breast cancer patients who possess risk factors for cancer of the corpus uteri (*21*). In an overall analysis, such as that presented in this monograph, the effect of such factors may be diluted. The excess risk of cancer in the uterus, NOS, may be an artifact due to increased medical attention because the risk became nonsignificant after the first year of observation was excluded and it decreased over time.

That the risks of second cancers of the liver and biliary tract were significantly below expectation may be due to underreporting or conservative coding practices in the Registry (*22*), especially because liver cancers are frequently regarded as metastases from the primary breast cancer. No explanation was apparent for the increased risk of malignant melanoma, although a similar association found in Connecticut suggests the possibility of a common hormonal etiology (*6*). Because of the number of computations done, however, it should be kept in mind that some results may be significant by chance alone.

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BREAST
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TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the breast, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	—	54,964	54,964
No. who developed a second primary cancer	—	2,480	2,480
Average age at diagnosis of first cancer, yr		60	60
Average yr of diagnosis of first cancer	—	1965	1965
Person-yr of follow-up	—	345,097	345,097
Average follow-up, yr	—	6.3	6.3
Percent given radiotherapy for first cancer		69	69

[a] ICD-7 code = 170. Male breast cancers are not included in this set of tables.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B. *Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the breast in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	2,008	79.9
Only the first cancer	385	15.3
Only the second cancer	92	3.7
Neither first nor second cancer	29	1.2
Total second primary cancers	2,514	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

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TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the breast among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	54,964			46,362			22,421			11,273			54,964		
Person-yr in interval	50,710			128,756			79,452			86,180			345,098		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**251**	**309.16**	**0.8**[b]	**811**	**818.58**	**1.0**	**601**	**547.16**	**1.1**[b]	**817**	**722.86**	**1.1**[b]	**2,480**	**2,397.75**	**1.0**
All excluding site of initial cancer	**251**	**309.16**	**0.8**[b]	**811**	**818.58**	**1.0**	**601**	**547.16**	**1.1**[b]	**817**	**722.86**	**1.1**[b]	**2,480**	**2,397.75**	**1.0**
Buccal cavity, pharynx	**2**	**5.23**	**0.4**	**10**	**13.80**	**0.7**	**13**	**9.21**	**1.4**	**16**	**12.23**	**1.3**	**41**	**40.46**	**1.0**
Lip	2	0.77	2.6	1	2.04	0.5	2	1.37	1.5	2	1.88	1.1	7	6.06	1.2
Tongue	0	0.92	0.0	2	2.39	0.8	2	1.58	1.3	1	2.10	0.5	5	6.99	0.7
Salivary gland	0	1.16	0.0	2	3.02	0.7	1	1.97	0.5	7	2.21	3.2[b]	10	8.37	1.2
Gum, other mouth	0	1.41	0.0	3	3.82	0.8	4	2.61	1.5	6	3.95	1.5	13	11.79	1.1
Pharynx	0	0.97	0.0	2	2.53	0.8	4	1.67	2.4	0	2.09	0.0	6	7.26	0.8
Digestive system	**105**	**130.87**	**0.8**[b]	**315**	**344.64**	**0.9**	**242**	**230.88**	**1.0**	**347**	**315.58**	**1.1**	**1,009**	**1,021.97**	**1.0**
Esophagus	1	3.71	0.3	6	9.56	0.6	7	6.34	1.1	15	8.65	1.7	29	28.25	1.0
Stomach	31	34.41	0.9	87	86.69	1.0	62	55.35	1.1	64	67.25	1.0	244	243.70	1.0
Colon	29	40.20	0.7	105	108.19	1.0	87	74.08	1.2	130	106.65	1.2[b]	351	329.11	1.1
Rectum	21	23.23	0.9	61	61.33	1.0	41	41.14	1.0	64	55.22	1.2	187	180.93	1.0
Liver, biliary	8	10.80	0.7	16	29.50	0.5[b]	17	20.58	0.8	21	30.71	0.7	62	91.59	0.7[b]
Pancreas	13	12.77	1.0	25	34.93	0.7	20	24.30	0.8	46	36.33	1.3	104	108.32	1.0
Respiratory system	**16**	**19.68**	**0.8**	**63**	**54.01**	**1.2**	**60**	**37.39**	**1.6**[b]	**82**	**53.41**	**1.5**[b]	**221**	**164.49**	**1.3**[b]
Nasal cavities, sinuses	1	0.60	1.7	1	1.56	0.6	0	1.03	0.0	0	1.36	0.0	2	4.56	0.4
Larynx	2	0.86	2.3	1	2.33	0.4	3	1.60	1.9	1	2.09	0.5	7	6.89	1.0
Trachea, bronchus, lung	13	16.56	0.8	57	45.78	1.2	53	31.84	1.7[b]	76	46.12	1.6[b]	199	140.30	1.4[b]
Female breast[c]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Female genital tract	**70**	**79.51**	**0.9**	**218**	**208.63**	**1.0**	**145**	**136.08**	**1.1**	**190**	**159.99**	**1.2**[b]	**623**	**584.20**	**1.1**
Cervix uteri	21	28.44	0.7	64	72.20	0.9	36	44.20	0.8	43	44.27	1.0	164	189.11	0.9
Corpus uteri	22	21.67	1.0	61	58.37	1.0	44	39.85	1.1	51	50.14	1.0	178	170.03	1.0
Uterus, NOS	5	1.75	2.9	9	4.30	2.1	5	2.68	1.9	1	3.13	0.3	20	11.85	1.7[b]
Ovary, fallopian tubes	21	22.92	0.9	75	61.19	1.2	50	40.91	1.2	76	51.07	1.5[b]	222	176.09	1.3[b]
Kidney, renal pelvis, ureter	10	9.90	1.0	34	26.82	1.3	24	18.46	1.3	29	25.72	1.1	97	80.91	1.2
Bladder, other urinary	10	10.35	1.0	30	28.27	1.1	19	19.65	1.0	23	28.52	0.8	82	86.79	0.9
Melanoma of the skin	6	5.56	1.1	24	14.98	1.6[b]	13	9.93	1.3	16	12.68	1.3	59	43.15	1.4[b]
Eye	2	1.10	1.8	3	2.90	1.0	1	1.94	0.5	3	2.38	1.3	9	8.31	1.1
Brain, central nervous system	4	7.83	0.5	20	20.87	1.0	14	13.96	1.0	13	17.49	0.7	51	60.16	0.8
Thyroid gland	3	2.63	1.1	9	7.02	1.3	7	4.72	1.5	4	6.39	0.6	23	20.76	1.1
Bone	0	0.68	0.0	2	1.72	1.2	5	1.10	4.6[b]	4	1.33	3.0	11	4.83	2.3[b]
Connective tissue	1	1.35	0.7	5	3.46	1.4	3	2.16	1.4	11	2.59	4.3[b]	20	9.56	2.1[b]
Lymphatic, hematopoietic system	**17**	**19.89**	**0.9**	**62**	**53.69**	**1.2**	**47**	**36.77**	**1.3**	**60**	**51.90**	**1.2**	**186**	**162.25**	**1.1**
Non-Hodgkin's lymphoma	6	5.90	1.0	16	16.02	1.0	7	11.04	0.6	21	15.89	1.3	50	48.85	1.0
Hodgkin's disease	1	1.52	0.7	1	3.97	0.3	2	2.60	0.8	2	3.24	0.6	6	11.32	0.5
Multiple myeloma	1	3.89	0.3	6	10.61	0.6	7	7.39	0.9	10	10.75	0.9	24	32.65	0.7
Leukemias	9	8.40	1.1	39	22.58	1.7[b]	29	15.40	1.9[b]	26	21.59	1.2	103	67.97	1.5[b]
Chronic lymphocytic	4	3.61	1.1	9	9.72	0.9	10	6.68	1.5	6	9.63	0.6	29	29.64	1.0
Acute nonlymphocytic	4	2.41	1.7	18	6.67	2.7[b]	13	4.65	2.8[b]	16	6.96	2.3[b]	51	20.69	2.5[b]

[a] ICD-7 code = 170.

[b] $P < .05$.

[c] Second breast cancers were not available on the Danish Cancer Registry computer files.

Second Cancer Following Cancer of the Female Genital System in Denmark, 1943–80 [1]

Hans H. Storm *and* Marianne Ewertz [2]

ABSTRACT—Between 1943 and 1980, approximately 53,000 women in Denmark survived 2 or more months after initial diagnoses of cancers of the cervix uteri, corpus uteri, ovaries, fallopian tubes, and ligaments. No significant excess of new cancers was observed following cancers of the cervix and corpus uteri. However, after second cancers of both the cervix and corpus uteri were eliminated from the analysis (because it was likely they were surgically removed or not recorded due to conservative coding practices), 6 and 4% excess risks of borderline significance were found among women with cancer of the cervix and uterus, respectively. A significant 25% excess of all second primary cancers was observed following cancer of the ovary (relative risk = 1.25; 95% CI = 1.14-1.37). Significant excesses of colon and breast cancers followed cancers of the ovary and corpus uteri. Subsequent to cervical cancer, the risk of cancers of the lung, esophagus, bladder, and kidney occurred significantly above expectation. These associations may be explained by common risk factors related to reproduction and possibly diet for cancers of the breast, colon, ovary, and corpus uteri; and to cigarette smoking for cancers of the lung, esophagus, bladder, and cervix uteri. The significant deficit of breast cancer after cervical cancer could be due to different patterns of risk factors (i.e., reproductive and socioeconomic variables) and loss of functioning ovaries as a part of the treatment for cervical cancer. Each of the female genital sites showed significant excesses of second bladder cancers, and the risk increased significantly with time, which indicate a relation to radiotherapy. The pattern of risk of leukemia observed following cancer of the ovary was also compatible with effects of treatment, especially chemotherapy.—Natl Cancer Inst Monogr 68: 331-340, 1985.

CERVIX UTERI (ICD-7, 171)

Cancer of the cervix, one of the most frequent malignant tumors affecting women in Denmark, accounted for 6% of all cancers among women in 1980. The age-standardized incidence rates peaked in the mid-1960s at 32/100,000 women, which was more than twice the rate observed in other Scandinavian countries. A steady decline in cervical cancer incidence was observed thereafter, reaching 18/100,000 women in 1980 (*1*). Part of the continued decrease in incidence may be explained by the effect of screening, although a change in the pattern of risk factors may be involved as well.

The risk factors reported for cervical cancer include low social class, early age at first intercourse, multiple sexual partners, marriage to someone with multiple sexual partners, and smoking of cigarettes (*2*). Cancer of the cervix has features of a sexually transmitted disease, with herpes virus type 2 and human papillomavirus suspected as causal agents.

About 80% of the cervical cancers were squamous cell carcinomas, 8% were adenocarcinomas (with a poorer prognosis), and 12% had other specified or unspecified morphology (*1*). The most important factor in prognosis is the extent of the disease when treatment is instituted and, secondly, the histologic type of cancer. The survival experience is generally favorable. Even if age at diagnosis and stage of disease are not taken into account, a 5-year relative survival rate as high as 71% has been reported (*3*). Treatment for cervical cancer has remained essentially unchanged for several decades: radiotherapy alone or in combination with surgery, or surgery alone, from simple hysterectomy to complete removal of the internal genital tract including regional lymph nodes.

Results

During the years 1943–80, the Registry was notified of 26,711 women with cancer of the cervix uteri who survived 2 or more months. These women contributed a total of 251,653 woman-years of observation. The average age at diagnosis was 50 years, and the average follow-up was 9.4 years. About 81% of the patients were irradiated as part of their initial treatment; approximately 15% had surgery alone, whereas 20% had surgery combined with radiotherapy. However, notification of treatment to the Registry is not accurate and radiotherapy tends to be underreported (*4*).

Second primary cancers developed in 1,576 (or 5.9%) patients. Of these, a high percentage (85%) had both the first and second primary cancers histologically confirmed. Although the validity of diagnoses based solely on death certification is not especially reliable (*5*), only 3% of the second cancers following cervical cancer were so classified by death certificates alone. The total expected numbers include those for second cervical cancer. Surgery for cervical cancer as well as reporting and registration practices in Denmark result in a low probability of a second primary cancer of the cervix developing or being recorded. When the observed and expected numbers of cervical cancers are subtracted from the totals, a significant excess of second cancer is seen (RR = 1.06; 95% CI = 1.01–1.12).

Significantly increased risks were observed for cancers

ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Hans H. Storm, M.D.

of the lung, esophagus, kidney, and urinary bladder. A significant deficit was observed for cancers of the breast and ovary throughout the follow-up period, whereas the deficit of cancer of the corpus uteri was only present in the first 10 years after initial diagnosis. Second primary cancer of the bone was excessive 5–9 years after the initial cervical cancer diagnosis (RR = 6.7; 95% CI = 1.8–17), whereas the risks of connective tissue and rectal cancers became significantly high 10 or more years after the initial diagnosis.

Discussion

A small (6%) but significantly increased risk of second cancers subsequent to cervical cancer was found. The site distribution and latency of these second cancers agree well with the results of other large-scale studies (*6, 7*). The observed deficit of breast cancer among patients with cervical cancer is consistent with the protective effect of surgical removal or radiation sterilization of the ovaries (*8, 9*). Risk factors for breast and cervical cancer also seem to operate in reverse, e.g., high socioeconomic status is associated with a high risk for breast cancer and a low risk for cervical cancer (*2*).

Interpretation of the risks associated with developing second cancers of other female genital organs is difficult. Firstly, the expected numbers should be based on the population-at-risk, with adjustment for removal of the uteri. Secondly, because cervical cancer frequently spreads within the female genital tract, second cancers within these organs are not likely to be accepted as new primary cancers. However, the increasing risk for second cancers of the corpus uteri and, to some extent, the ovary, might be due to radiation therapy. A portion of the elevated risks for cancers of the lung, kidney, and bladder may be attributable to misclassification of metastases, but the high percentage of histologically verified cases makes this an unlikely explanation for the large increases. A common risk factor, cigarette smoking, may be involved in cancers of the lung, bladder, and kidney. The excess risk for bladder, rectum, and kidney cancers could also be associated with radiation treatment. The persistent risk for kidney cancer may also be explained in part by a higher autopsy rate among cancer patients and the identification of second cancers at autopsy (*5*). Our findings are consistent with previous studies (*6, 7*). The nonsignificant excess risk of ANLL 1–4 years after diagnosis is compatible with a radiation effect (*10*). More detailed studies of cervical cancer patients, with treatment and organs at risk taken into account, are underway in Denmark as part of a large international collaborative effort (*7*).

CORPUS UTERI (ICD-7, 172)

Cancer of the corpus uteri represents about 5% of all malignant neoplasms in women in Denmark. Between 1943 and 1980, the age-standardized incidence rate rose steadily and almost doubled (*11*). The predominant host factors are obesity, nulliparity, and late age at menopause. Dietary fat, estrogen replacement therapy, and pelvic irradiation constitute exogenous factors (*2*). During the past 20 years, survival after cancer of the corpus uteri has increased about 10%; the overall 5-year relative survival rate is about 75% in the Scandinavian countries (*3, 12*). The prognosis depends on age at diagnosis (younger patients have a more favorable prognosis than do older patients) and stage of disease. Five-year relative survival rates range from 85% for localized tumors to 20% for tumors with distant metastases (*3*).

Results

After having been diagnosed with cancer of the corpus uteri between 1943 and 1980, 13,370 women survived 2 or more months. The average age at diagnosis was 61 years, and the average follow-up was 8.2 years. The initial treatment involved surgery in 71% (hysterectomy and probably oophorectomy) and radiation in 57% of the women.

A total of 958 patients (or 7.2%) developed a second primary cancer. Two of these, located in the corpus uteri, were probably misclassified metastases and were therefore excluded; thus 956 cases were available for analysis. On the basis of the rates in the general population, 1,030 second cancers were expected. To correct for the loss of the cervix, corpus uteri, and ovaries at surgery, we deducted 71% of the expected contribution from these organs, which yielded an adjusted expected number of 897. Compared with the observed number, the RR was 1.07 (95% CI = 0.99–1.14).

Significant excess risks were found for cancers of the breast, colon, and bladder; these sites accounted for 50% of all second tumors. Among 4,348 patients surviving 10 or more years, the risks were significantly elevated for second cancers of the colon and bladder. The risk of rectal cancer increased significantly with time. There was a significant deficit of stomach cancer that persisted 10 years or more after the initial diagnosis. Of the female genital organs, the risk of cervical cancer remained significantly reduced after correction for hysterectomy, whereas the RR of ovarian cancer changed from 0.8 (95% CI = 0.6–1.0) to 2.7 (95% CI = 2.0–3.6) when allowance was made for decreased numbers at risk.

Discussion

Women with cancer of the corpus uteri had no greater incidence of subsequent cancer than did the general population. For certain sites, however, risks were found both above and below expectation. Cancer of the corpus uteri may spread directly to the bladder and rectum, and it is possible that the excess risk of bladder cancer after 1–4 years of follow-up was due to misclassification of metastases. More than one-half the patients were treated initially with radiation, whereby the bladder and rectum may have been exposed (*13*). Minimum latency for radiation-induced solid tumors have been estimated to be about 10 years (*14*), so the elevated risks of bladder and rectal cancers after 10 or more years of observation are consistent with a radiation effect. An increased risk of leukemia (1.3) subsequent to treatment for cancer of the corpus uteri was recently reported (*15*). This level of risk was similar to our findings for all types of leukemia, but neither result reached statistical significance.

The risk of second breast cancer was not increased as much as in other studies (*16–18*). It was significantly elevated only during the 1–4 years after the first primary diagnosis and did not increase with time. This may reflect the influence of increased medical attention. The relationship between cancer of the corpus uteri and subsequent breast cancer may be due to associated risk factors (*16*), which increase the breast cancer risk in a subgroup of patients. Common etiologic factors related to diet have also been suggested for cancers of the corpus uteri and colon (*2*). The association between cancers of these 2 sites is much stronger in the present data than previously reported (*16, 18*). Dietary factors and possibly differences in social class (*19*) may have been involved in reducing the risk of a person developing a second cancer of the stomach.

The evaluation of second cancers in the female genital organs is difficult because 1) the population-at-risk is not clearly defined and 2) metastases from cancer of the corpus uteri may arise in other organs in the female genital tract. The latter reason may explain the excess risk of ovarian cancer seen in the first year after the diagnosis of uterine corpus cancer.

OVARY (ICD-7, 175)

Cancers of the ovary also include rare tumors of the fallopian tubes and broad ligaments. These sites represent 4% of all malignant neoplasms in women in Denmark. The age-standardized incidence rate in Denmark increased steadily between 1943 and 1977, leveling off in 1980 to 15/100,000 women. An increasing incidence for ovarian cancer is observed in other countries as well (*20*).

The survival after cancer of the ovary is poor with all ages and stages combined, and the 5-year relative survival rate is about 37% (*3*). Treatment for ovarian cancer usually includes surgery, but 34% received radiation as well. In recent years, cancer chemotherapy, especially with alkylating agents, has been used often in combination with surgery (*21, 22*).

Little is known about the origins of ovarian cancer, but nulliparity has been consistently observed as a risk factor. Other possible risk factors include high fat diet, exogenous estrogens, and never being married (*2*). The reason for the apparent differences in risk factors in various studies could be due to the complex morphologic types of ovarian cancer. Perhaps separate consideration of the three main types (epithelial, germ cell, and sex-cord stromal tumors) would be worthwhile, but small numbers have prohibited such an evaluation.

Previous studies of multiple primary cancers following cancer of the ovary have reported elevated risks for cancers of the colon, endometrium, and breast (*6, 16*). These associations have been attributed to common risk factors such as high fat diet or to treatment with radiation (*2*).

Results

In the 1943- to 1980-period, 12,758 women contributed 48,260 woman-years of observation after initial diagnoses of cancer in the ovaries, fallopian tubes, and ligaments. The average follow-up time was 3.8 years, and the mean age at diagnosis was 58 years. Second primary cancers were observed in 455 women compared with 365 expected (RR = 1.25; 95% CI = 1.14–1.37). The excess risk appeared at all periods after initial diagnosis, but it was not statistically significant 10 years or more after diagnosis.

A significant decrease in risk over time was present for cancer of the digestive organs ($P = .002$ for trend). A significant excess risk of colon cancer (RR = 1.7; 95% CI = 1.3–2.2) was found, whereas the risk for cancer of the rectum was elevated, though not significantly (RR = 1.4; 95% CI = 0.9–2.0). Cancers of the breast and corpus uteri were increased 1–9 years after the initial diagnosis of ovarian cancer. The risk of a second primary bladder cancer increased significantly over time ($P < .001$ for trend) with a large excess (15 observed versus 3.9 expected) seen 10 or more years after the initial diagnosis. Kidney cancer occurred excessively in the first 5 years of observation. The leukemias, largely confined to the acute types, showed an elevated risk overall (RR = 1.9; 95% CI = 1.0–3.1), but the excess was concentrated in the 1- to 4-year follow-up period. Only 1 site, the cervix, showed a deficit in all periods (RR = 0.6; 95% CI = 0.3–0.97).

Discussion

Overall, ovarian cancer patients showed a significant 25% excess of all second primary cancers. The lack of an increased risk of breast cancer 10 or more years after diagnosis is puzzling because cancers of the ovary and breast are thought to share some risk factors. However, the finding may be related to the surgical removal of the ovaries, which is known to protect against breast cancer development.

The excess risk of second cancers in the corpus uteri may reflect misclassification of metastases or the influence of common risk factors. The increased risk of kidney cancer is likely attributed to the close medical surveillance of ovarian cancer patients including x rays, urograms, and perhaps a more frequent rate of autopsies than performed in the general population. The colon cancer excess is unlikely to be due solely to the misclassification of metastases, and common risk factors are probably involved. The increased risk of leukemia, especially ANLL, has been linked to alkylating agents in a Danish series which is included in this cohort (*22*). Further studies are needed for clarification of the risks and determinants of bladder and kidney cancers.

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CERVIX
FEMALES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the cervix uteri, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	0	26,711	26,711
No. who developed a second primary cancer	0	1,576	1,576
Average age at diagnosis of first cancer, yr	0	50	50
Average yr of diagnosis of first cancer	0	1962	1962
Person-yr of follow-up	0	251,653	251,653
Average follow-up, yr	0	9.4	9.4
Percent given radiotherapy for first cancer	0	81	81

[a] ICD-7 code = 171.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the cervix uteri in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	1,342	85.2
Only the first cancer	193	12.3
Only the second cancer	39	2.5
Neither first nor second cancer	2	0.1
Total second primary cancers	1,576	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

CERVIX
FEMALES

TABLE 1C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the cervix uteri among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	26,711			22,295			13,957			10,248			26,711		
Person-yr in interval	24,712			67,642			59,752			99,548			251,653		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**75**	**118.12**	**0.6**[b]	**325**	**340.64**	**1.0**	**320**	**349.90**	**0.9**	**856**	**822.17**	**1.0**	**1,576**	**1,630.83**	**1.0**
All excluding site of initial cancer	**75**	**103.04**	**0.7**[b]	**323**	**298.36**	**1.1**	**319**	**312.32**	**1.0**	**856**	**765.94**	**1.1**[b]	**1,573**	**1,479.66**	**1.1**[b]
Buccal cavity, pharynx	**2**	**1.43**	**1.4**	**1**	**4.05**	**0.2**	**6**	**4.15**	**1.4**	**16**	**10.33**	**1.5**	**25**	**19.96**	**1.3**
Lip	0	0.20	0.0	1	0.55	1.8	0	0.58	0.0	3	1.53	2.0	4	2.86	1.4
Tongue	0	0.21	0.0	0	0.58	0.0	0	0.61	0.0	2	1.64	1.2	2	3.05	0.7
Salivary gland	0	0.44	0.0	0	1.22	0.0	1	1.14	0.9	3	2.04	1.5	4	4.84	0.8
Gum, other mouth	1	0.30	3.3	0	0.87	0.0	3	0.97	3.1	3	3.09	1.0	7	5.23	1.3
Pharynx	1	0.28	3.5	0	0.81	0.0	2	0.85	2.4	5	2.03	2.5	8	3.98	2.0
Digestive system	**14**	**30.04**	**0.5**[b]	**98**	**84.07**	**1.2**	**88**	**88.38**	**1.0**	**288**	**240.44**	**1.2**[b]	**488**	**442.94**	**1.1**[b]
Esophagus	2	0.74	2.7	7	1.98	3.5[b]	4	2.08	1.9	8	5.91	1.4	21	10.71	2.0[b]
Stomach	2	7.42	0.3[b]	16	19.37	0.8	18	18.88	1.0	58	44.66	1.3	94	90.33	1.0
Colon	3	9.35	0.3[b]	35	26.89	1.3	31	29.14	1.1	91	83.67	1.1	160	149.06	1.1
Rectum	2	5.93	0.3	9	16.83	0.5	15	17.53	0.9	68	45.27	1.5[b]	94	85.55	1.1
Liver, biliary	1	2.32	0.4	10	6.81	1.5	4	7.65	0.5	20	23.56	0.8	35	40.33	0.9
Pancreas	2	2.86	0.7	14	8.44	1.7	12	9.49	1.3	33	29.03	1.1	61	49.82	1.2
Respiratory system	**10**	**5.23**	**1.9**	**69**	**15.96**	**4.3**[b]	**63**	**18.26**	**3.5**[b]	**97**	**51.60**	**1.9**[b]	**239**	**91.05**	**2.6**[b]
Nasal cavities, sinuses	0	0.17	0.0	0	0.50	0.0	0	0.52	0.0	5	1.25	4.0[b]	5	2.43	2.1
Larynx	0	0.26	0.0	2	0.81	2.5	2	0.91	2.2	5	2.29	2.2	9	4.27	2.1
Trachea, bronchus, lung	10	4.39	2.3[b]	66	13.53	4.9[b]	60	15.64	3.8[b]	84	45.06	1.9[b]	220	78.62	2.8[b]
Female breast	18	28.56	0.6[b]	61	83.82	0.7[b]	68	85.71	0.8	138	184.95	0.7[b]	285	383.03	0.7[b]
Female genital tract	**9**	**32.05**	**0.3**[b]	**21**	**92.40**	**0.2**[b]	**24**	**89.93**	**0.3**[b]	**105**	**174.67**	**0.6**[b]	**159**	**389.06**	**0.4**[b]
Cervix uteri	0	15.08	0.0[b]	2	42.28	0.0[b]	1	37.58	0.0[b]	0	56.23	0.0[b]	3	151.17	0.0[b]
Corpus uteri	3	7.25	0.4	2	21.71	0.1[b]	7	23.21	0.3[b]	43	53.83	0.8	55	105.99	0.5[b]
Uterus, NOS	1	0.48	2.1	1	1.21	0.8	1	1.09	0.9	1	2.20	0.5	4	4.98	0.8
Ovary, fallopian tubes	5	8.01	0.6	13	23.67	0.5[b]	7	24.39	0.3[b]	32	53.10	0.6[b]	57	109.18	0.5[b]
Kidney, renal pelvis, ureter	6	2.59	2.3	12	7.73	1.6	11	8.51	1.3	30	22.94	1.3	59	41.77	1.4[b]
Bladder, other urinary	6	2.45	2.5	18	7.29	2.5[b]	19	8.23	2.3[b]	82	24.16	3.4[b]	125	42.11	3.0[b]
Melanoma of the skin	2	2.08	1.0	4	6.32	0.6	7	6.56	1.1	11	14.21	0.8	24	29.18	0.8
Eye	0	0.37	0.0	1	1.05	1.0	3	1.06	2.8	4	2.28	1.8	8	4.75	1.7
Brain, central nervous system	2	3.05	0.7	9	8.91	1.0	6	9.02	0.7	15	19.31	0.8	32	40.29	0.8
Thyroid gland	0	0.74	0.0	2	2.14	0.9	1	2.22	0.5	6	5.43	1.1	9	10.52	0.9
Bone	1	0.23	4.3	0	0.63	0.0	4	0.59	6.7[b]	1	1.18	0.9	6	2.63	2.3
Connective tissue	0	0.48	0.0	1	1.33	0.8	2	1.22	1.6	7	2.47	2.8[b]	10	5.51	1.8
Lymphatic, hematopoietic system	**3**	**5.45**	**0.6**	**23**	**15.82**	**1.5**	**17**	**16.75**	**1.0**	**36**	**44.49**	**0.8**	**79**	**82.51**	**1.0**
Non-Hodgkin's lymphoma	1	1.56	0.6	7	4.58	1.5	5	4.99	1.0	12	13.88	0.9	25	25.01	1.0
Hodgkin's disease	0	0.63	0.0	4	1.74	2.3	2	1.61	1.2	3	3.21	0.9	9	7.19	1.3
Multiple myeloma	0	0.95	0.0	1	2.81	0.4	0	3.14	0.0	8	9.01	0.9	9	15.90	0.6
Leukemias	2	2.26	0.9	11	6.51	1.7	9	6.82	1.3	11	17.96	0.6	33	33.55	1.0
Chronic lymphocytic	1	0.80	1.2	4	2.29	1.7	3	2.46	1.2	6	7.19	0.8	14	12.75	1.1
Acute nonlymphocytic	1	0.70	1.4	5	2.12	2.4	4	2.33	1.7	4	6.51	0.6	14	11.67	1.2

[a] ICD-7 code = 171.
[b] $P < .05$.

CORPUS
FEMALES

Table 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the corpus uteri (excluding uterus, NOS), 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	0	13,370	13,370
No. who developed a second primary cancer	0	958	958
Average age at diagnosis of first cancer, yr	0	61	61
Average yr of diagnosis of first cancer	0	1965	1965
Person-yr of follow-up	0	110,029	110,029
Average follow-up, yr	0	8.2	8.2
Percent given radiotherapy for first cancer	0	57	57

[a] ICD-7 code = 172.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

Table 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the corpus uteri (excluding uterus, NOS) in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	805	84.0
Only the first cancer	109	11.4
Only the second cancer	39	4.1
Neither first nor second cancer	5	0.5
Total second primary cancers	958	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

CORPUS
FEMALES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the corpus uteri (excluding uterus, NOS) among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	13,370			11,143			6,818			4,348			13,370		
Person-yr in interval	12,260			34,152			27,139			36,479			110,029		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**68**	**95.90**	**0.7**[b]	**253**	**274.61**	**0.9**	**233**	**240.59**	**1.0**	**404**	**418.48**	**1.0**	**958**	**1,029.58**	**0.9**[b]
All excluding site of initial cancer	**68**	**89.70**	**0.8**[b]	**253**	**256.66**	**1.0**	**233**	**225.29**	**1.0**	**403**	**396.14**	**1.0**	**957**	**967.79**	**1.0**
Buccal cavity, pharynx	**1**	**1.25**	**0.8**	**3**	**3.56**	**0.8**	**2**	**3.13**	**0.6**	**4**	**5.71**	**0.7**	**10**	**13.65**	**0.7**
Lip	0	0.18	0.0	1	0.52	1.9	2	0.48	4.2	0	0.95	0.0	3	2.13	1.4
Tongue	0	0.21	0.0	0	0.59	0.0	0	0.52	0.0	1	0.96	1.0	1	2.27	0.4
Salivary gland	1	0.29	3.5	0	0.82	0.0	0	0.69	0.0	0	0.99	0.0	1	2.79	0.4
Gum, other mouth	0	0.32	0.0	1	0.94	1.1	0	0.86	0.0	2	1.90	1.1	3	4.03	0.7
Pharynx	0	0.24	0.0	1	0.69	1.5	0	0.58	0.0	1	0.92	1.1	2	2.43	0.8
Digestive system	**16**	**29.79**	**0.5**[b]	**78**	**85.06**	**0.9**	**91**	**77.17**	**1.2**	**171**	**150.18**	**1.1**	**356**	**342.19**	**1.0**
Esophagus	0	0.77	0.0	5	2.16	2.3	1	1.96	0.5	4	3.97	1.0	10	8.86	1.1
Stomach	2	7.10	0.3	9	19.45	0.5[b]	13	16.87	0.8	20	30.59	0.7	44	74.02	0.6[b]
Colon	6	9.39	0.6	40	27.26	1.5[b]	49	25.24	1.9[b]	72	51.48	1.4[b]	167	113.36	1.5[b]
Rectum	0	5.58	0.0[b]	10	15.98	0.6	11	14.31	0.8	36	26.01	1.4	57	61.87	0.9
Liver, biliary	3	2.58	1.2	7	7.58	0.9	5	7.24	0.7	13	15.19	0.9	28	32.59	0.9
Pancreas	4	3.10	1.3	5	9.13	0.5	10	8.64	1.2	25	17.93	1.4	44	38.81	1.1
Respiratory system	**2**	**5.07**	**0.4**	**17**	**14.95**	**1.1**	**22**	**13.65**	**1.6**[b]	**27**	**24.93**	**1.1**	**68**	**58.60**	**1.2**
Nasal cavities, sinuses	0	0.15	0.0	0	0.43	0.0	2	0.38	5.3	0	0.62	0.0	2	1.58	1.3
Larynx	0	0.23	0.0	0	0.66	0.0	1	0.57	1.8	1	0.91	1.1	2	2.36	0.8
Trachea, bronchus, lung	2	4.32	0.5	16	12.80	1.2	19	11.74	1.6	22	21.61	1.0	59	50.47	1.2
Female breast	20	20.97	1.0	84	59.71	1.4[b]	62	50.89	1.2	94	82.99	1.1	260	214.56	1.2[b]
Female genital tract	**17**	**20.80**	**0.8**	**21**	**59.16**	**0.4**[b]	**15**	**48.89**	**0.3**[b]	**19**	**69.81**	**0.3**[b]	**72**	**198.66**	**0.4**[b]
Cervix uteri	1	7.01	0.1[b]	1	19.40	0.1[b]	2	14.85	0.1[b]	4	17.66	0.2[b]	8	58.92	0.1[b]
Corpus uteri	0	6.20	0.0[b]	0	17.95	0.0[b]	0	15.30	0.0[b]	1	22.34	0.0[b]	1	61.79	0.0[b]
Uterus, NOS	1	0.37	2.7	0	0.99	0.0	0	0.80	0.0	0	1.33	0.0	1	3.49	0.3
Ovary, fallopian tubes	13	6.11	2.1[b]	17	17.61	1.0	10	15.08	0.7	9	23.09	0.4[b]	49	61.88	0.8
Kidney, renal pelvis, ureter	3	2.51	1.2	4	7.35	0.5	4	6.71	0.6	12	12.16	1.0	23	28.73	0.8
Bladder, other urinary	1	2.53	0.4	19	7.45	2.6[b]	10	6.98	1.4	23	13.86	1.7[b]	53	30.81	1.7[b]
Melanoma of the skin	3	1.35	2.2	3	3.92	0.8	4	3.38	1.2	10	5.54	1.8	20	14.19	1.4
Eye	0	0.29	0.0	1	0.83	1.2	2	0.72	2.8	1	1.11	0.9	4	2.95	1.4
Brain, central nervous system	1	2.13	0.5	4	6.18	0.6	3	5.26	0.6	10	7.65	1.3	18	21.22	0.8
Thyroid gland	0	0.63	0.0	1	1.82	0.5	3	1.65	1.8	2	3.04	0.7	6	7.15	0.8
Bone	0	0.16	0.0	1	0.46	2.2	0	0.39	0.0	2	0.62	3.2	3	1.63	1.8
Connective tissue	0	0.33	0.0	1	0.92	1.1	0	0.76	0.0	1	1.21	0.8	2	3.22	0.6
Lymphatic, hematopoietic system	**3**	**4.91**	**0.6**	**16**	**14.35**	**1.1**	**13**	**13.19**	**1.0**	**24**	**24.85**	**1.0**	**56**	**57.31**	**1.0**
Non-Hodgkin's lymphoma	1	1.45	0.7	5	4.27	1.2	3	3.95	0.8	5	7.61	0.7	14	17.29	0.8
Hodgkin's disease	0	0.38	0.0	1	1.08	0.9	1	0.95	1.1	1	1.49	0.7	3	3.90	0.8
Multiple myeloma	0	0.98	0.0	1	2.90	0.3	0	2.73	0.0	6	5.20	1.2	7	11.82	0.6
Leukemias	2	2.05	1.0	9	5.95	1.5	9	5.45	1.7	11	10.34	1.1	31	23.79	1.3
Chronic lymphocytic	1	0.85	1.2	3	2.45	1.2	2	2.28	0.9	7	4.60	1.5	13	10.17	1.3
Acute nonlymphocytic	1	0.62	1.6	1	1.84	0.5	3	1.72	1.7	0	3.38	0.0	5	7.55	0.7

[a] ICD-7 code = 172.

[b] $P < .05$.

OVARY
FEMALES

TABLE 3A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the ovary or fallopian tubes, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	0	12,758	12,758
No. who developed a second primary cancer	0	455	455
Average age at diagnosis of first cancer, yr	0	58	58
Average yr of diagnosis of first cancer	0	1965	1965
Person-yr of follow-up	0	48,260	48,260
Average follow-up, yr	0	3.8	3.8
Percent given radiotherapy for first cancer	0	34	34

[a] ICD-7 code = 175.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the ovary or fallopian tubes in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	386	84.8
Only the first cancer	43	9.5
Only the second cancer	19	4.2
Neither first nor second cancer	7	1.5
Total second primary cancers	455	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

OVARY
FEMALES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the ovary or fallopian tubes among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	12,758			6,614			2,652			1,555			12,758		
Person-yr in interval	9,365			15,278			10,141			13,477			48,260		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**84**	**63.46**	**1.3^b**	**142**	**101.96**	**1.4^b**	**97**	**74.13**	**1.3^b**	**132**	**125.44**	**1.1**	**455**	**364.99**	**1.2^b**
All excluding site of initial cancer	**83**	**59.35**	**1.4^b**	**139**	**95.37**	**1.5^b**	**95**	**69.46**	**1.4^b**	**130**	**118.12**	**1.1**	**447**	**342.31**	**1.3^b**
Buccal cavity, pharynx	**0**	**0.81**	**0.0**	**1**	**1.29**	**0.8**	**1**	**0.95**	**1.1**	**5**	**1.65**	**3.0**	**7**	**4.70**	**1.5**
Lip	0	0.12	0.0	0	0.18	0.0	1	0.14	7.1	2	0.25	8.0	3	0.69	4.3
Tongue	0	0.13	0.0	0	0.21	0.0	0	0.15	0.0	1	0.28	3.6	1	0.77	1.3
Salivary gland	0	0.20	0.0	1	0.31	3.2	0	0.22	0.0	1	0.30	3.3	2	1.03	1.9
Gum, other mouth	0	0.20	0.0	0	0.33	0.0	0	0.26	0.0	1	0.53	1.9	1	1.32	0.8
Pharynx	0	0.16	0.0	0	0.25	0.0	0	0.18	0.0	0	0.29	0.0	0	0.88	0.0
Digestive system	**37**	**18.80**	**2.0^b**	**45**	**29.89**	**1.5^b**	**32**	**22.49**	**1.4**	**41**	**41.30**	**1.0**	**155**	**112.48**	**1.4^b**
Esophagus	0	0.48	0.0	1	0.76	1.3	1	0.58	1.7	0	1.09	0.0	2	2.91	0.7
Stomach	6	4.44	1.4	8	6.86	1.2	3	4.99	0.6	4	8.27	0.5	21	24.56	0.9
Colon	14	5.96	2.3^b	19	9.63	2.0^b	12	7.38	1.6	19	14.22	1.3	64	37.19	1.7^b
Rectum	5	3.55	1.4	8	5.62	1.4	5	4.16	1.2	10	7.34	1.4	28	20.66	1.4
Liver, biliary	4	1.62	2.5	1	2.63	0.4	2	2.07	1.0	3	4.08	0.7	10	10.40	1.0
Pancreas	7	1.95	3.6^b	0	3.17	0.0	6	2.47	2.4	3	4.88	0.6	16	12.47	1.3
Respiratory system	**5**	**3.28**	**1.5**	**9**	**5.39**	**1.7**	**6**	**4.06**	**1.5**	**7**	**7.53**	**0.9**	**27**	**20.26**	**1.3**
Nasal cavities, sinuses	0	0.10	0.0	0	0.16	0.0	0	0.11	0.0	1	0.19	5.3	1	0.55	1.8
Larynx	1	0.15	6.7	0	0.25	0.0	0	0.18	0.0	0	0.30	0.0	1	0.88	1.1
Trachea, bronchus, lung	4	2.79	1.4	9	4.60	2.0	6	3.48	1.7	6	6.54	0.9	25	17.41	1.4
Female breast	12	14.32	0.8	35	23.14	1.5^b	22	16.48	1.3	18	26.56	0.7	87	80.50	1.1
Female genital tract	**16**	**14.43**	**1.1**	**28**	**23.13**	**1.2**	**21**	**15.99**	**1.3**	**17**	**23.43**	**0.7**	**82**	**76.98**	**1.1**
Cervix uteri	4	5.37	0.7	4	8.65	0.5	3	5.64	0.5	5	7.05	0.7	16	26.71	0.6^b
Corpus uteri	11	3.99	2.8^b	18	6.39	2.8^b	15	4.56	3.3^b	7	7.15	1.0	51	22.10	2.3^b
Uterus, NOS	0	0.24	0.0	2	0.36	5.5	1	0.26	3.9	1	0.39	2.6	4	1.24	3.2
Ovary, fallopian tubes	1	4.11	0.2	3	6.59	0.5	2	4.67	0.4	2	7.32	0.3^b	8	22.68	0.4^b
Kidney, renal pelvis, ureter	5	1.61	3.1^b	7	2.60	2.7^b	1	1.95	0.5	7	3.52	2.0	20	9.67	2.1^b
Bladder, other urinary	1	1.61	0.6	3	2.63	1.1	3	2.03	1.5	15	3.88	3.9^b	22	10.16	2.2^b
Melanoma of the skin	0	0.98	0.0	2	1.65	1.2	3	1.19	2.5	1	1.94	0.5	6	5.76	1.0
Eye	0	0.19	0.0	1	0.30	3.3	0	0.22	0.0	0	0.33	0.0	1	1.04	1.0
Brain, central nervous system	1	1.46	0.7	1	2.38	0.4	1	1.67	0.6	3	2.58	1.2	6	8.09	0.7
Thyroid gland	0	0.42	0.0	1	0.67	1.5	0	0.50	0.0	4	0.87	4.6^b	5	2.46	2.0
Bone	0	0.11	0.0	1	0.18	5.6	1	0.12	8.2	0	0.18	0.0	2	0.59	3.4
Connective tissue	1	0.23	4.4	0	0.35	0.0	0	0.24	0.0	1	0.37	2.7	2	1.19	1.7
Lymphatic, hematopoietic system	**3**	**3.21**	**0.9**	**7**	**5.20**	**1.3**	**6**	**3.90**	**1.5**	**12**	**7.09**	**1.7**	**28**	**19.40**	**1.4**
Non-Hodgkin's lymphoma	1	0.94	1.1	1	1.54	0.6	2	1.17	1.7	5	2.18	2.3	9	5.84	1.5
Hodgkin's disease	0	0.27	0.0	0	0.45	0.0	0	0.32	0.0	1	0.47	2.1	1	1.51	0.7
Multiple myeloma	0	0.63	0.0	0	1.01	0.0	1	0.77	1.3	2	1.44	1.4	3	3.85	0.8
Leukemias	2	1.33	1.5	6	2.15	2.8^b	3	1.61	1.9	4	2.93	1.4	15	8.03	1.9^b
Chronic lymphocytic	2	0.53	3.8	0	0.86	0.0	0	0.65	0.0	0	1.26	0.0	2	3.31	0.6
Acute nonlymphocytic	0	0.41	0.0	3	0.68	4.4	1	0.52	1.9	2	0.99	2.0	6	2.61	2.3

[a] ICD-7 code = 175.

[b] $P < .05$.

Second Cancer Following Cancer of the Male Genital System in Denmark, 1943–80 [1]

Anne Østerlind, [2] Mikael Rørth, [3] *and* Anne Prener [2]

ABSTRACT—The incidence of second primary cancers was investigated among 19,886 patients with prostate cancer. The analysis disclosed 594 new cancers, which was significantly less than the expected 1,176 cases (relative risk = 0.51). Deficits were observed for most sites but were only significant for cancers of the lip, lung, and gastrointestinal organs. The average age at diagnosis of prostate cancer was 72 years. It is likely that the apparent deficit in the incidence of second neoplasms resulted from less diagnostic aggressiveness in elderly patients with cancer compared with younger patients. The risk of developing a second primary cancer was also investigated in 4,290 men with testis cancer reported to the Danish Cancer Registry between 1943 and 1980. A significant 29% excess of second cancers was found (174 observed vs. 135 expected). A bimodal distribution of risk over time was found with a 67% excess seen among patients followed for 1–4 years that was mainly due to increased incidence of acute nonlymphocytic leukemia and malignant lymphomas. Among patients surviving 10 or more years, the overall excess of 32% observed was mainly due to cancers of the gastrointestinal tract and the urinary bladder. As part of the initial treatment for testis cancer, 82% of the patients received radiotherapy. Chemotherapy was rarely given before 1975 and then mostly to patients with a poor prognosis. Late effects of radiotherapy conceivably could account for some of the excess of second hematologic as well as solid neoplasms.—Natl Cancer Inst Monogr 68: 341–347, 1985.

PROSTATE (ICD-7, 177)

Prostate cancer is the second most frequent cancer in men, constituting 10% of all cancers in males in Denmark. The age standardized incidence rate is 28/100,000 man-years (*1*) and has increased over time since 1943 (*2*). Prostate cancer appears late in life, and the pattern of increasing incidence with age is more prominent than for any other cancer. Possible etiologic factors include the hormone dependency of the prostate, relationship to high sexual activity, fat consumption, and occupational exposure to cadmium (*3*). The incidence of clinical prostate cancer varies widely among different populations of the world (*4*), with the lowest rates in Shanghai and Japan (0.8 and 3.4/100,000 man-years, respectively) and the highest in the black population of Alameda County, California (100/100,000 man-years).

Many reports have shown unrecognized "latent" or "occult" carcinoma of the prostate to be far more common than clinically apparent prostate cancer (*3*). The calculated survival rate depends heavily on the diagnosis and inclusion of these latent carcinomas in the Registry material. In 1972–75, the 5-year relative survival rate in Norway was 52% and has increased significantly in past decades. This increase apparently cannot be explained by changes in age or stage distribution alone (*5*). The survival rate in Denmark is probably comparable but would depend strongly on whether the number of latent carcinomas included in the 2 registries was similar.

Results

During 1943–80, of the 19,886 men with clinically apparent prostate cancer who were reported to the Registry and fulfilled the criteria for inclusion in the study cohort, 11% received radiotherapy as initial treatment either alone or in combination with surgery or surgery and other treatment, 28% were treated with surgery alone, and 35% received other treatment alone, e.g., estrogen therapy. The average age at time of diagnosis was 72 years, and the average follow-up was 3.2 years.

A total of 594 (or 3.0%) of the patients with prostate cancer developed a second cancer compared with 1,176 expected on the basis of rates in the general population (RR = 0.51; 95% CI = 0.47–0.55). The deficit of second tumors was constant throughout all intervals and was especially noticeable for cancers of the digestive organs (RR = 0.5; 95% CI = 0.5–0.6) and respiratory system (RR = 0.5; 95% CI = 0.4–0.6). A significant deficit of second cancers of the buccal cavity and pharynx was also observed, with the most prominent deficit seen for lip cancers (7 vs. 17.7).

No single site showed a significant increased risk above that expected on the basis of rates generated from the population in general. Sites with elevated risks, although not significant, included melanoma of the skin, cancer of connective tissue, and Hodgkin's disease. Of these, the most interesting is melanoma of the skin, with an RR of 1.8 (95% CI = 1.0–3.0). The risk remained elevated throughout all intervals after the first year of observation. Eight of the 14 melanomas were reported 1–4 years after the initial diagnosis.

Discussion

The number of reported second cancers in men with prostate cancer was significantly lower than expected,

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ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia.

[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Anne Østerlind, M.D.

[3] Department of Oncology II, Finsen Institute, Strandboulevarden 49, DK-2100 Copenhagen, Denmark.

especially for cancers of the gastrointestinal and respiratory organs. Similar findings emerged from a previous investigation of second primary cancers in Connecticut (*6*). Before exploring further the biologic reasons for this finding, one should consider the possibility of underreporting or lack of diagnostic aggressiveness. It may be that because of the advanced age of patients with prostate cancer, i.e., 72 years on average, the possibility of a second cancer is of less concern to attending physicians than among younger patients. In addition, if the rates of autopsy among elderly individuals are lower, the chance of detecting new cancers is also lessened.

Because a high proportion of the men (60%) with prostate cancer could have received estrogen therapy, the elevated risk for melanoma of the skin is worth investigating. For example, oral contraceptives may be related to the development of malignant melanoma in women (*7*).

TESTIS (ICD-7, 178)

Testis cancer, which accounts for 1.8% of all malignant diseases in Danish men, is the most frequent cancer among men 15–44 years old and represents 23% of all cancer detected in this age category. The age-standardized incidence rate increased from 3.1 to 8.2/100,000 man-years between 1943 and 1980 (*1, 2*). The increase was seen for seminomas and nonseminomas (other germ cell neoplasms combined) almost to the same degree (*8*). As pointed out by Clemmesen (*9*), Denmark has the highest reported age-adjusted incidence of testis cancer in the world (*4*). The cumulative risk of testis cancer (from birth to age 44 yr) is 4/1,000.

The etiology of testis cancer is unknown. However, risk factors identified in epidemiology studies include cryptorchism, high social class, and professional occupations. Associations have also been suggested for inguinal hernia, testicular injury, maternal use of exogenous estrogens during pregnancy, mumps orchitis, marital status, urban residence, and certain religions (*10–12*).

Of the reported testis cancers in Denmark during 1978–80, 55% were seminomas and 45% were nonseminomas. The same ratio of the 2 histologic groups has been observed in various other countries (*13*) and has remained fairly constant in Denmark during the last 30 years over which the incidence has more than doubled. Until recently, major prognostic differences existed between seminomas and nonseminomas; i.e., survival rates for all stages of nonseminomas were much lower than for seminomas. The difference in the biologic behavior of these 2 histologies is further reflected in the higher proportion of distant metastases occurring in patients with nonseminomas. Recent reports from the Danish Testicular Carcinoma Study Group and other groups have demonstrated improved prognosis of patients with nonseminomatous tumors due to the introduction of combination chemotherapy with *cis*-platinum. As a consequence of these therapeutic improvements, testis cancer is now among the most curable cancers in men. In Danish patients diagnosed from 1979 to 1983, the crude 4-year survival of patients with seminomas was above 90% and for patients with nonseminomas above 80% (*14, 15*), compared with 70% and 27%, respectively, in the period from 1935 to 1957 (*16*).

Results

Presently, data on 4,290 men diagnosed with testis cancer in Denmark between 1943 and 1980 are included in Registry files. These men lived at least 2 months after diagnosis without developing a second primary cancer. The average age at diagnosis was 38 years, and the average follow-up was 8.3 years. The initial therapy included surgery 90% of the time and radiation 82% of the time. A total of 174 (or 4.1%) of these patients developed a second primary tumor, of whom 98% had histologic verification of the testis cancer, and 87% histologic verification of the testis and subsequent cancers. On the basis of rates in the general population, 135 new cancers were expected (RR = 1.29; 95% CI = 1.11–1.49). An excess of subsequent cancers of the urinary bladder, including papillomas, was seen (RR = 1.8; 95% CI = 1.1–2.7), and the risk increased significantly over time ($P < .001$ for trend) due to an excess appearing 10 years or more after initial diagnosis. Cancer of the contralateral testis was diagnosed in excess (RR = 3.4; 95% CI = 1.7–6.1), with most second testis cancers diagnosed 5 or more years after the initial diagnosis. To reduce the possibility that cancers in the contralateral testis were metastases, we did not include those cases for which the morphology of primary and secondary tumors were alike.

Significant excess risk was observed for cancers of the digestive organs taken as a group (RR = 1.4), although no individual site was significantly elevated. More than 70% of the tumors of the digestive organs occurred 10 years or more after the initial diagnosis of testis cancer ($P < .0001$ for trend). Relatively high observed-to-expected ratios were found for bone and connective tissue tumors, but the numbers were small and the ratios were not significantly different from unity.

An increased risk for leukemia was suggested, mainly due to a significant excess of ANLL 1–4 years after diagnosis (RR = 12.6; 95% CI = 2.5–37). A similar result was seen for non-Hodgkin's lymphoma during the same follow-up period (RR = 7.3; 95% CI = 2.0–19). The risks of ANLL and non-Hodgkin's lymphoma, however, did not reach the level of statistical significance when all intervals were considered. No cancer of any site occurred significantly below expectation based on general population rates.

Discussion

The testis cancer patients in this survey had significantly more new cancers than expected on the basis of our comparison with the general population. Cancers of the digestive organs, bladder, and contralateral testis accounted for 50% of all second cancers. The risk over time had a bimodal distribution with a 67% excess seen among patients surviving 1–4 years after initial diagnosis and a 32% excess among patients surviving 10 or more years. The risks in the first year after the diagnosis of testis cancer and in years 5–9 were consistent with expectation.

The first peak is due mainly to neoplams of the lymphatic and hematopoietic systems. According to Boice (*17*), leukemia is one of the most commonly found tumors associated with radiation; thus radiotherapy for testis cancer, which often includes irradiating the lymph nodes in the abdominal area, may be related to a portion of the observed ANLL excess. Our present results agree with the slightly increased risk of ANLL following testis cancer that was recently reported (*18*).

Inasmuch as 82% of the patients with testis cancer received radiotherapy as initial treatment, the bladder and several gastrointestinal organs (stomach, colon, rectum) were exposed to varying doses. The minimum period for development of radiation-induced solid tumors has been estimated to be about 10 years (*16*). The significantly elevated risks after 10 or more years from initial treatment of the testis cancer suggests that radiation is involved in the etiology of these second neoplasms.

The threefold risk for cancer of the contralateral testis should be considered a minimum estimate. The risk was significantly elevated only in years 5–9 after the primary diagnosis and did not increase with time. Whether the excess risk is due to the initial treatment, to risk factors shared with the primary testis tumor, or to increased patient and physician awareness cannot be determined from this study.

The use of chemotherapy has increased in recent years and before 1975 was generally restricted to patients with nonseminomatous tumors with extension of the disease beyond the local site. Only a small fraction of these patients survived for long enough periods to be at risk of developing a second primary cancer. The effect of modern chemotherapy (after 1975) for testis cancer on the development of second cancers is not known because the available observation time is still fairly short. Furthermore, the combination chemotherapy regimens used in Denmark do not include alkylating agents, which have been shown to be leukemogenic. A detailed evaluation of patients subjected to standardized and well-defined treatment regimens may give an answer to this important problem, although case–control studies of registered patients might also provide useful information. The possible risk of radiation-induced secondary cancers could be evaluated likewise from careful analysis of the treatment (radiation quality, intensity, fields) and tumor characteristics (histology, anatomic location in relation to the field of irradiation) of patients with testis cancer. Treatment-induced cancer is a potentially serious concern because many patients are cured and live for a long time after they were diagnosed as having testis cancer.

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PROSTATE
MALES

TABLE 1A. *Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the prostate gland, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	19,886	0	19,886
No. who developed a second primary cancer	594	0	594
Average age at diagnosis of first cancer, yr	72	0	72
Average yr of diagnosis of first cancer	1967	0	1967
Person-yr of follow-up	62,900	0	62,900
Average follow-up, yr	3.2	0	3.2
Percent given radiotherapy for first cancer	11	0	11

[a] ICD-7 code = 177.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the prostate gland in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	420	70.7
Only the first cancer	75	12.6
Only the second cancer	68	11.5
Neither first nor second cancer	31	5.2
Total second primary cancers	594	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

PROSTATE
MALES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the prostate gland among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	19,886			13,904			4,025			1,080			19,886		
Person-yr in interval	16,720			30,796			10,992			4,393			62,900		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**110**	**287.52**	**0.4**[b]	**295**	**560.81**	**0.5**[b]	**124**	**223.71**	**0.6**[b]	**65**	**104.16**	**0.6**[b]	**594**	**1,176.21**	**0.5**[b]
All excluding site of initial cancer	**110**	**241.66**	**0.5**[b]	**295**	**468.95**	**0.6**[b]	**124**	**184.89**	**0.7**[b]	**65**	**84.67**	**0.8**[b]	**594**	**980.18**	**0.6**[b]
Buccal cavity, pharynx	**4**	**8.32**	**0.5**	**11**	**15.76**	**0.7**	**2**	**6.00**	**0.3**	**0**	**2.64**	**0.0**	**17**	**32.72**	**0.5**[b]
Lip	0	4.52	0.0[b]	6	8.55	0.7	1	3.25	0.3	0	1.42	0.0	7	17.74	0.4[b]
Tongue	0	0.64	0.0	0	1.20	0.0	1	0.44	2.3	0	0.17	0.0	1	2.45	0.4
Salivary gland	0	0.68	0.0	0	1.29	0.0	0	0.50	0.0	0	0.22	0.0	0	2.69	0.0
Gum, other mouth	1	1.23	0.8	4	2.37	1.7	0	0.93	0.0	0	0.46	0.0	5	4.99	1.0
Pharynx	3	1.26	2.4	1	2.35	0.4	0	0.87	0.0	0	0.37	0.0	4	4.84	0.8
Digestive system	**51**	**113.39**	**0.4**[b]	**117**	**218.82**	**0.5**[b]	**50**	**87.75**	**0.6**[b]	**26**	**41.20**	**0.6**[b]	**244**	**461.16**	**0.5**[b]
Esophagus	2	4.96	0.4	5	9.27	0.5	2	3.57	0.6	0	1.58	0.0	9	19.37	0.5[b]
Stomach	20	36.30	0.6[b]	44	68.52	0.6[b]	12	27.02	0.4[b]	6	12.23	0.5	82	144.08	0.6[b]
Colon	14	26.50	0.5[b]	27	52.27	0.5[b]	12	21.64	0.6[b]	7	10.87	0.6	60	111.28	0.5[b]
Rectum	4	24.86	0.2[b]	19	47.82	0.4[b]	17	18.97	0.9	8	8.68	0.9	48	100.33	0.5[b]
Liver, biliary	3	6.13	0.5	6	12.25	0.5	1	5.05	0.2	2	2.48	0.8	12	25.91	0.5[b]
Pancreas	8	11.27	0.7	10	22.32	0.4[b]	5	9.04	0.6	3	4.26	0.7	26	46.88	0.6[b]
Respiratory system	**15**	**51.71**	**0.3**[b]	**50**	**100.97**	**0.5**[b]	**17**	**38.17**	**0.4**[b]	**10**	**15.96**	**0.6**	**92**	**206.82**	**0.4**[b]
Nasal cavities, sinuses	0	0.74	0.0	2	1.41	1.4	0	0.55	0.0	0	0.25	0.0	2	2.95	0.7
Larynx	3	3.34	0.9	2	6.42	0.3	2	2.40	0.8	3	1.01	3.0	10	13.17	0.8
Trachea, bronchus, lung	11	45.04	0.2[b]	45	88.06	0.5[b]	15	33.15	0.5[b]	7	13.74	0.5	78	179.98	0.4[b]
Prostate gland	0	45.86	0.0[b]	0	91.86	0.0[b]	0	38.82	0.0[b]	0	19.49	0.0[b]	0	196.03	0.0[b]
Testis	0	0.55	0.0	2	1.02	2.0	1	0.38	2.7	0	0.17	0.0	3	2.12	1.4
Kidney, renal pelvis, ureter	8	8.94	0.9	15	17.53	0.9	6	7.00	0.9	6	3.27	1.8	35	36.74	1.0
Bladder, other urinary	16	22.94	0.7	49	45.33	1.1	20	18.12	1.1	10	8.53	1.2	95	94.92	1.0
Melanoma of the skin	1	1.96	0.5	8	3.80	2.1	3	1.48	2.0	2	0.71	2.8	14	7.94	1.8
Eye	0	0.77	0.0	2	1.47	1.4	0	0.56	0.0	0	0.25	0.0	2	3.05	0.7
Brain, central nervous system	1	3.20	0.3	4	6.00	0.7	1	2.11	0.5	2	0.81	2.5	8	12.13	0.7
Thyroid gland	1	0.75	1.3	1	1.45	0.7	0	0.57	0.0	1	0.25	4.0	3	3.03	1.0
Bone	0	0.47	0.0	0	0.89	0.0	0	0.35	0.0	1	0.15	6.7	1	1.86	0.5
Connective tissue	0	0.90	0.0	1	1.68	0.6	4	0.65	6.2[b]	0	0.30	0.0	5	3.51	1.4
Lymphatic, hematopoietic system	**9**	**18.07**	**0.5**[b]	**30**	**35.59**	**0.8**	**18**	**14.28**	**1.3**	**5**	**6.72**	**0.7**	**62**	**74.65**	**0.8**
Non-Hodgkin's lymphoma	2	4.49	0.4	5	8.80	0.6	3	3.48	0.9	1	1.59	0.6	11	18.36	0.6
Hodgkin's disease	2	1.00	2.0	1	1.90	0.5	3	0.72	4.2	0	0.32	0.0	6	3.93	1.5
Multiple myeloma	1	3.44	0.3	2	6.82	0.3	4	2.76	1.4	1	1.29	0.8	8	14.31	0.6
Leukemias	4	8.97	0.4	21	17.74	1.2	8	7.20	1.1	3	3.46	0.9	36	37.35	1.0
Chronic lymphocytic	2	5.18	0.4	11	10.26	1.1	5	4.20	1.2	1	2.04	0.5	19	21.67	0.9
Acute nonlymphocytic	1	2.03	0.5	6	4.09	1.5	1	1.67	0.6	1	0.80	1.2	9	8.59	1.0

[a] ICD-7 code = 177.

[b] $P < .05$.

TESTIS
MALES

TABLE 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the testis, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	4,290	0	4,290
No. who developed a second primary cancer	174	0	174
Average age at diagnosis of first cancer, yr	38	0	38
Average yr of diagnosis of first cancer	1966	0	1966
Person-yr of follow-up	35,778	0	35,778
Average follow-up, yr	8.3	0	8.3
Percent given radiotherapy for first cancer	82	0	82

[a] ICD-7 code = 178.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the testis in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	151	86.8
Only the first cancer	19	10.9
Only the second cancer	4	2.3
Neither first nor second cancer	0	0.0
Total second primary cancers	174	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

TESTIS
MALES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the testis among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,290			3,434			2,056			1,362			4,290		
Person-yr in interval	3,886			10,195			8,441			13,256			35,778		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**3**	**7.32**	**0.4**	**36**	**21.62**	**1.7**[b]	**27**	**24.79**	**1.1**	**108**	**81.66**	**1.3**[b]	**174**	**135.39**	**1.3**[b]
All excluding site of initial cancer	**3**	**6.90**	**0.4**	**33**	**20.52**	**1.6**[b]	**22**	**23.97**	**0.9**	**105**	**80.75**	**1.3**[b]	**163**	**132.14**	**1.2**[b]
Buccal cavity, pharynx	**0**	**0.32**	**0.0**	**1**	**0.97**	**1.0**	**1**	**1.08**	**0.9**	**3**	**2.98**	**1.0**	**5**	**5.35**	**0.9**
Lip	0	0.18	0.0	0	0.54	0.0	0	0.59	0.0	1	1.55	0.6	1	2.85	0.4
Tongue	0	0.02	0.0	0	0.07	0.0	1	0.08	12.7	0	0.22	0.0	1	0.39	2.6
Salivary gland	0	0.03	0.0	0	0.10	0.0	0	0.10	0.0	0	0.24	0.0	0	0.48	0.0
Gum, other mouth	0	0.03	0.0	0	0.10	0.0	0	0.12	0.0	0	0.42	0.0	0	0.69	0.0
Pharynx	0	0.05	0.0	1	0.16	6.1	0	0.19	0.0	2	0.55	3.6	3	0.95	3.2
Digestive system	**0**	**2.27**	**0.0**	**6**	**6.47**	**0.9**	**10**	**7.48**	**1.3**	**40**	**24.61**	**1.6**[b]	**56**	**40.82**	**1.4**[b]
Esophagus	0	0.10	0.0	0	0.29	0.0	0	0.33	0.0	3	1.11	2.7	3	1.83	1.6
Stomach	0	0.70	0.0	1	1.89	0.5	3	2.08	1.4	11	6.00	1.8	15	10.66	1.4
Colon	0	0.51	0.0	2	1.48	1.3	3	1.74	1.7	8	6.07	1.3	13	9.81	1.3
Rectum	0	0.51	0.0	2	1.47	1.4	2	1.71	1.2	10	5.73	1.7	14	9.42	1.5
Liver, biliary	0	0.11	0.0	0	0.34	0.0	2	0.42	4.8	2	1.65	1.2	4	2.53	1.6
Pancreas	0	0.24	0.0	1	0.72	1.4	0	0.89	0.0	5	3.22	1.6	6	5.07	1.2
Respiratory system	**1**	**1.43**	**0.7**	**3**	**4.61**	**0.7**	**4**	**5.84**	**0.7**	**22**	**21.72**	**1.0**	**30**	**33.59**	**0.9**
Nasal cavities, sinuses	0	0.03	0.0	0	0.08	0.0	0	0.09	0.0	0	0.27	0.0	0	0.47	0.0
Larynx	0	0.12	0.0	0	0.40	0.0	0	0.50	0.0	3	1.68	1.8	3	2.70	1.1
Trachea, bronchus, lung	1	1.21	0.8	3	3.94	0.8	3	5.02	0.6	18	19.06	0.9	25	29.24	0.9
Prostate gland	0	0.51	0.0	2	1.36	1.5	1	1.68	0.6	10	7.63	1.3	13	11.19	1.2
Testis	0	0.42	0.0	3	1.10	2.7	5	0.82	6.1[b]	3	0.91	3.3	11	3.25	3.4[b]
Kidney, renal pelvis, ureter	0	0.25	0.0	3	0.78	3.8	0	0.95	0.0	0	3.13	0.0	3	5.11	0.6
Bladder, other urinary	0	0.54	0.0	1	1.67	0.6	4	2.07	1.9	16	7.71	2.1[b]	21	11.99	1.8[b]
Melanoma of the skin	0	0.18	0.0	2	0.56	3.6	0	0.57	0.0	3	1.29	2.3	5	2.61	1.9
Eye	0	0.03	0.0	0	0.10	0.0	0	0.11	0.0	0	0.29	0.0	0	0.54	0.0
Brain, central nervous system	0	0.34	0.0	0	1.02	0.0	1	1.05	1.0	1	2.40	0.4	2	4.80	0.4
Thyroid gland	0	0.03	0.0	0	0.09	0.0	0	0.10	0.0	1	0.28	3.6	1	0.50	2.0
Bone	1	0.04	26.4	0	0.10	0.0	0	0.08	0.0	1	0.16	6.3	2	0.37	5.4
Connective tissue	0	0.05	0.0	0	0.15	0.0	1	0.14	7.0	2	0.31	6.5	3	0.66	4.6
Lymphatic, hematopoietic system	**1**	**0.68**	**1.5**	**12**	**1.94**	**6.2**[b]	**0**	**2.04**	**0.0**	**3**	**5.79**	**0.5**	**16**	**10.46**	**1.5**
Non-Hodgkin's lymphoma	1	0.18	5.4	4	0.55	7.3[b]	0	0.59	0.0	1	1.68	0.6	6	3.00	2.0
Hodgkin's disease	0	0.15	0.0	2	0.39	5.1	0	0.33	0.0	0	0.61	0.0	2	1.48	1.3
Multiple myeloma	0	0.08	0.0	0	0.24	0.0	0	0.29	0.0	0	1.01	0.0	0	1.61	0.0
Leukemias	0	0.26	0.0	5	0.75	6.7[b]	0	0.81	0.0	2	2.43	0.8	7	4.25	1.6
Chronic lymphocytic	0	0.10	0.0	0	0.28	0.0	0	0.33	0.0	0	1.15	0.0	0	1.85	0.0
Acute nonlymphocytic	0	0.08	0.0	3	0.24	12.6[b]	0	0.25	0.0	1	0.77	1.3	4	1.34	3.0

[a] ICD-7 code = 178.
[b] $P < .05$.

Second Cancer Following Cancer of the Urinary System in Denmark, 1943–80 [1]

Ole M. Jensen, [2] Jens B. Knudsen, [3] *and* Bent L. Sørensen [3]

ABSTRACT—**The risk of second primary cancer was evaluated in 29,128 patients who developed tumors of the urinary tract, including benign and malignant tumors of the renal pelvis and ureter and bladder papillomas in Denmark between 1943 and 1980. Among 9,162 persons with kidney cancer, 416 developed a second primary tumor [relative risk (RR) = 1.4]. Among 19,966 persons with bladder cancer, 1,423 developed a second primary tumor against 1,239 expected (RR = 1.1). The risk of bladder cancer was increased following kidney cancer in both men (RR = 6.3) and women (RR = 10.1), and kidney cancer was increased in both men (RR = 2.9) and women (RR = 4.5) following bladder cancer. These risks were particularly pronounced for cancers occurring in the ureter and renal pelvis. Etiologic similarities are likely explanations for these observations, which also emphasize the role of host factors and the multifocal nature of urothelial tumors. A decrease in relative risks since diagnosis of the first primary cancer was seen that may partly be attributed to a lessening of the intensity of medical surveillance with time. Among long-term survivors with kidney cancer, increased risks were observed for colon and pancreatic cancers, which may be related to treatment; approximately 25% received radiotherapy. Among bladder cancer patients, increased risks of cancers of the lung and larynx occurred, probably due to tobacco smoking. A slight elevation of prostate cancer (RR = 1.3) may be attributable to medical surveillance. Unexpected findings were the significant deficits of cancers of the stomach and rectum among patients with bladder cancer and stomach cancer among those with kidney cancer.—Natl Cancer Inst Monogr 68: 349–360, 1985.**

KIDNEY, RENAL PELVIS, AND URETER (ICD-7, 180)

Cancers of the kidney encompass a heterogeneous group of tumors, both with regard to tissue of origin and possible etiology. The Danish modification of the ICD-7 includes as kidney cancer any malignant neoplasm of the kidney parenchyma, kidney NOS, and tumors of the renal pelvis and of the ureter, irrespective of whether these latter 2 are benign or malignant (*1*). The Registry records multiple tumors of the bladder, ureter, and renal pelvis in the same person as multiple primary cancers. Each diagnosis appears as an independent tumor record on the Registry file, although multiple tumors in paired organs are included only once.

Tumors of the renal pelvis and ureter accounted for 22% of the 9,162 kidney cancers included in the present study. A review of hospital records of tumors recorded as kidney NOS in 1955 and in 1975 indicated that more than 95% of the classifiable tumors in this group arose from the kidney parenchyma.

A total of 3.4% of all tumors in Denmark occur in the kidney. The age-standardized incidence rates are 9.2/100,000 for men and 6.6/100,000 for women; the risk is thus 1.4 times higher for men than for women. (*1*). Differences have been noted in the time trends of the component tumors of the kidney, with sharp increases in tumors of the renal pelvis and ureter, but only a slight increase in the incidence of cancer of the renal parenchyma (hypernephroma or adenocarcinoma). No increase in kidney parenchymal tumors is seen during the period from 1965 to 1980 (Knudsen JB, Geser A, Jensen OM: Personal communication).

Risk factors are likely to be different for renal pelvis and ureteral tumors and renal cell adenocarcinomas of the kidney. All urothelial-derived tumors are thought to be influenced by the same risk factors, the most important of which is tobacco smoking, particularly cigarettes (*2–5*). A small number of tumors may be attributable to industrial exposures. Other suspected risk factors such as coffee consumption and the use of artificial sweeteners have not been corroborated by recent Danish studies (*5, 6*). The risk of tumors of the renal pelvis is influenced by the use of analgesics containing phenacetin (*7*). Comparisons of the epidemiology of bladder cancer and cancer of the renal pelvis and ureter in Denmark indicate that risk factors may differ; e.g., the male-to-female ratio in the latter group is much smaller than for bladder cancer, and the increase over time is steeper and more recent (Knudsen JB, Geser A, Jensen OM: Personal communication).

Few factors have been suggested to influence the development of cancers arising from the kidney parenchyma. The risks associated with tobacco smoking and with obesity (especially in females) appear well established (*8, 9*); persons of German and North European descent seem to be at increased risk. Another influence could be radiation and possibly radioactive iodine because of the excess risk reported after treatment of hyperthyroidism (*10*). Wilms' tumor in childhood constitutes 1–2% of the total group, and second tumors developing among these as a result of radiotherapy (*11*) are unlikely to emerge in the type of analysis presented here.

ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; NOS = not otherwise specified; RR = relative risk(s); CI = confidence interval.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Ole M. Jensen, M.D.

[3] Department of Surgery, Finsen Institute, Strandboulevarden 49, DK-2100 Copenhagen, Denmark.

Results

A total of 9,162 persons with cancers of the kidney and tumors of the ureter and renal pelvis were included in the present study (5,122 males and 4,040 females). The average age at diagnosis was 61 years and the mean year of diagnosis was 1966. Survival is good for patients with these tumors, and the average follow-up was 3.3 years, which provided 30,371 person-years of observation. Almost 70% of the patients had undergone surgical intervention either alone or in combination with radiotherapy. Radiotherapy was given to 23% of the patients as part of their initial treatment. Of the 416 persons who developed a second primary tumor, 83% had both the kidney cancer and the second primary cancer histologically confirmed.

Among 5,122 men, 255 developed a second primary tumor (RR = 1.5; 95% CI = 1.3–1.6). Exclusion of the observed and expected tumors of the kidney, ureter, and renal pelvis did not affect the risk estimate. However, all of the excess could be ascribed to second bladder cancers (RR = 6.3; 95% CI = 5.1–7.7). The increased RR (5–10) of bladder cancer among men was seen during the first 10 years of follow-up and then fell to 1.1 among long-term survivors.

A total of 161 second primary cancers developed in the 4,040 women (RR = 1.2; 95% CI = 1.0–1.4). The overall risk estimate was not affected by the exclusion of observed and expected kidney tumors. As in men, the risk of bladder cancer was substantially increased (RR = 10.1; 95% CI = 7.2–14). Bladder cancer was elevated during all intervals of follow-up, including 10 or more years after diagnosis of the initial kidney cancer (RR = 3.9). Males showed a significant increased risk of connective tissue tumors (RR = 5.3; 95% CI = 1.1–16) which was not observed among females. A significantly increased risk of chronic lymphocytic leukemia was seen among women (RR = 4.4; 95% CI = 1.6–9.6) but not among men. A significant deficit of stomach cancer was observed for both sexes combined (RR = 0.5; 95% CI = 0.3–0.8). Among persons followed for 10 or more years after kidney cancer diagnoses, the RR of colon cancer (1.8) was almost double that expected on the basis of rates prevailing in the general population. The RR of pancreatic cancer (2.3) also was high. However, neither of these risk estimates was significantly different from 1.

Discussion

Persons with kidney cancer, which in Denmark includes benign and malignant tumors of the renal pelvis and ureter, have a significantly increased risk of developing a second tumor, particularly during the first 10 years of survival. The excess of approximately 110 tumors out of 416 observed is explained by a sevenfold increase in the risk of developing cancer of the urinary bladder, including papillomas. Because 22% of all kidney tumors are derived from the urothelium of the renal pelvis and the ureter, this finding points to the existence of common risk factors for transitional cell tumors and the tendency for multifocal neoplasms of the lower urinary tract to develop (*12*). Host susceptibility to urothelial tumors either alone or in combination with exogenous factors such as tobacco may play a role. Metabolic activation of tobacco combustion products has been suggested as one such possible mechanism (*13, 14*). The increased risk of bladder tumors may also be influenced by cystoscopic surveillance of patients with cancer of the renal pelvis and ureter, whereas patients treated for hypernephroma are not routinely followed with cystoscopy. The tendency of a decreasing RR with time may thus reflect a more intense follow-up with cystoscopy during the first years after a kidney cancer diagnosis.

Among long-term survivors, the risk of both colon and pancreatic cancers was increased about twofold. Although the increased risk is not statistically significant, it is possible that radiotherapy influenced the development of tumors at these sites, inasmuch as increased risks for cancers of the pancreas and colon have appeared among spondylitics treated with ionizing radiation (*15, 16*). In view of the association between kidney tumors, including the ureter and renal pelvis, and tobacco smoking (*8*), it is noteworthy that no increased risk is seen for cancer of the respiratory organs.

BLADDER INCLUDING PAPILLOMA (ICD-7, 181)

Since the start of the Danish Cancer Registry in 1942, all tumors of the bladder have been notifiable irrespective of whether they were benign or malignant (*17*). This was in part due to the difficulty encountered by physicians in determining whether a bladder tumor is invasive or not (*18*) and the assumption that an untreated papilloma of the bladder will often progress to an invasive, malignant tumor. Etiologic studies rarely distinguish between papilloma and invasive bladder tumors.

Comparisons on an international level are hampered by the difficulties in delineation of bladder cancer (*19*). When comparisons of incidence rates are restricted to areas which consider benign and malignant tumors of the bladder together, Denmark has an unusually high incidence of this disease (*20*). Bladder cancer accounts for 8.2% of all cancers in men and 2.6% in women. The age-standardized incidence rates are 23.4 and 6.1/100,000 in men and women, respectively. Rates recorded in Copenhagen are three times higher than in Danish rural areas. A continuous increase in incidence rates has been recorded since 1943 (*21*).

In the 1950s, the pattern of bladder cancer in Denmark was suggested to be due to tobacco smoking (*2*). Cigarette smoking in particular was confirmed as the most important risk factor by an early case-control study in Copenhagen (*3*), and the association has been found elsewhere (*22*). These findings were later confirmed by investigators in Copenhagen (*5*) and in a Danish rural area (*4*) showing that smoking of tobacco, particularly cigarettes, is by far the most important risk factor for bladder cancer in Denmark. Risk factors also include certain occupational exposures [(*4*); Jensen OM, Knudsen JB, Wahrendorf J, et al: Unpublished observations]. Although coffee consumption is high in Denmark, as in the rest of Scandinavia (two times higher than in the United States), the high bladder cancer risk in Denmark cannot be explained by this habit (*4, 23*).

Results

Bladder cancer was reported in 19,966 persons (15,236 men and 4,730 women) between 1943 and 1980 in Denmark. The average age at diagnosis was 66 years, and the average follow-up was 4.7 years with little difference between the 2 sexes. There were 94,799 person-years of observation, of which 19% were contributed by persons followed for 10 years or more. Slightly more than 90% of the index bladder cancers were histologically verified in persons who developed a second primary cancer. Both the first and second primary cancers were histologically confirmed 80% of the time. Approximately 90% of all second cancers were confirmed by a histologic examination (87.7%) or by autopsy alone (2.7%). According to the records available to the Registry, surgical treatment, primarily transurethral resection, was the predominant initial therapy for tumor management. Radiotherapy was given to 34% of the persons as an initial course of treatment. In all, 1,423 second primary cancers developed compared with 1,239 expected (RR = 1.15; 95% CI = 1.09–1.21). The excess of 184 cases diminished to 134, when the observed and expected numbers of bladder tumors were disregarded.

In both sexes the highest risk, excluding subsequent bladder cancer, was for cancer of the kidney (males: RR = 2.9; 95% CI = 2.4–3.6; females: RR = 4.5; 95% CI = 3.1–6.4), which included cancer of the ureter and renal pelvis as discussed above. The risk was characterized by being independent of the time since diagnosis of the bladder cancer. If anything, the RR decreased slightly with the highest risk being recorded within the first 5 years of the bladder cancer diagnosis. A further analysis covering the period from 1943 to 1977 showed that the risk of developing a second primary kidney cancer was mainly due to tumors derived from the urothelium of the renal pelvis and ureter, whereas the risk of tumors of the kidney parenchyma (including NOS) was increased only in the first year after the bladder cancer diagnosis.

Among males, significantly increased risks were noted for primary lung cancer development (RR = 1.6; 95% CI = 1.4–1.8). Increased risks of borderline significance were seen for cancer of the larynx (1.5; 95% CI = 0.9–2.2). For both sites, RR at the same level were noted among women but did not attain statistical significance. In males, the RR of lung cancer development was high, irrespective of time since bladder cancer diagnosis. The risk estimates for women were more irregular with time since diagnosis of the first primary than for men, probably due to the smaller number of tumors which occurred among women.

The RR of prostate cancer was slightly but significantly increased (1.3; 95% CI = 1.1–1.5). The highest RR was recorded immediately after the diagnosis of the bladder cancer, with no significant increases in subsequent follow-up periods. Significant or borderline deficits occurred in both sexes combined for cancers of the stomach (RR = 0.6; 95% CI = 0.5–0.8), rectum (RR = 0.8; 95% CI = 0.6–1.0), and brain (RR = 0.6; 95% CI = 0.3–1.0). The RR of cancer of the corpus uteri was 0.4 (95% CI = 0.1–0.9). Cancer development at other sites did not differ significantly from expectation, neither totally nor among long-term survivors.

Discussion

A large proportion of cancer of the bladder is attributable to environmental factors. The most important of these in Denmark is smoking, particularly cigarettes (*2–5*). Thus a larger proportion of smokers occurs among bladder cancer patients than among the general population. Against this background, it is not surprising that we find an increased risk of cancer of the lung and larynx in both sexes. The increased risks, independent of time since the bladder cancer diagnosis, suggest that cancers of the bladder, lung, and larynx have similar etiologies. The present findings are consistent with the associations between the incidence of lung and bladder cancers based on international comparisons (*24*).

The most frequent sites for new tumors among persons with bladder cancer are other parts of the urinary tract. Cancer of the kidney, including ureter and renal pelvis, occurred 3.2 times more frequently than expected, primarily due to urothelial tumors of the ureter and renal pelvis. This finding points to common risk factors with bladder cancer and confirms the clinical experience that tumor development of the urothelium may be regarded as a generalized multifocal process (*12*) and often involves the entire lower urinary tract.

Increased susceptibility of bladder cancer patients to develop urothelial tumors in other parts of the urinary tract may be related to the suggested mechanism for metabolic activation of carcinogens in tobacco smoke (*13, 14*). A certain proportion of the kidney cancers, particularly of the parenchyma, may be ascribed to routine urologic examinations, including urograms, which patients with bladder tumors undergo. Also, the increased risk of prostate cancer, particularly seen during the first year after bladder cancer diagnosis, may be attributed to intense urologic examination rather than biologic factors. In this context, one should note that no distinction is made between latent and symptomatic prostate cancer by the Danish Cancer Registry. The significant deficits seen for cancers of the stomach and rectum were not expected. However, the deficit of rectal cancer could be an artifact if clinicians interpreted tumors of the rectum as local extensions of a previous bladder cancer.

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KIDNEY
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the kidney, renal pelvis, or ureter, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	5,122	4,040	9,162
No. who developed a second primary cancer	255	161	416
Average age at diagnosis of first cancer, yr	61	61	61
Average yr of diagnosis of first cancer	1966	1966	1966
Person-yr of follow-up	16,125	14,246	30,371
Average follow-up, yr	3.2	3.5	3.3
Percent given radiotherapy for first cancer	24	22	23

[a] ICD-7 code = 180.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the kidney, renal pelvis, or ureter in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	346	83.2
Only the first cancer	43	10.3
Only the second cancer	20	4.8
Neither first nor second cancer	7	1.7
Total second primary cancers	416	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

KIDNEY
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the kidney, renal pelvis, or ureter among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	9,162			4,841			1,933			912			9,162		
Person-yr in interval	6,630			11,705			6,758			5,279			30,371		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**78**	**61.56**	**1.3**[b]	**181**	**112.76**	**1.6**[b]	**86**	**70.75**	**1.2**	**71**	**62.80**	**1.1**	**416**	**307.85**	**1.4**[b]
All excluding site of initial cancer	**72**	**59.64**	**1.2**	**179**	**109.19**	**1.6**[b]	**82**	**68.52**	**1.2**	**70**	**60.85**	**1.2**	**403**	**298.18**	**1.4**[b]
Buccal cavity, pharynx	**2**	**1.54**	**1.3**	**1**	**2.74**	**0.4**	**0**	**1.64**	**0.0**	**0**	**1.34**	**0.0**	**3**	**7.25**	**0.4**
Lip	1	0.70	1.4	0	1.23	0.0	0	0.71	0.0	0	0.54	0.0	1	3.20	0.3
Tongue	0	0.15	0.0	0	0.26	0.0	0	0.16	0.0	0	0.15	0.0	0	0.71	0.0
Salivary gland	0	0.17	0.0	0	0.30	0.0	0	0.18	0.0	0	0.15	0.0	0	0.80	0.0
Gum, other mouth	0	0.26	0.0	0	0.48	0.0	0	0.30	0.0	0	0.29	0.0	0	1.33	0.0
Pharynx	1	0.26	3.8	1	0.46	2.2	0	0.28	0.0	0	0.22	0.0	2	1.22	1.6
Digestive system	**8**	**21.54**	**0.4**[b]	**37**	**38.43**	**1.0**	**23**	**24.40**	**0.9**	**28**	**22.46**	**1.2**	**96**	**106.82**	**0.9**
Esophagus	0	0.81	0.0	1	1.40	0.7	0	0.88	0.0	0	0.77	0.0	1	3.86	0.3
Stomach	2	6.04	0.3	8	10.10	0.8	2	6.24	0.3	2	5.50	0.4	14	27.87	0.5[b]
Colon	0	5.64	0.0[b]	14	10.43	1.3	8	6.84	1.2	12	6.67	1.8	34	29.57	1.1
Rectum	4	4.50	0.9	7	8.00	0.9	4	4.97	0.8	3	4.36	0.7	18	21.82	0.8
Liver, biliary	0	1.48	0.0	5	2.83	1.8	1	1.87	0.5	3	1.84	1.6	9	8.02	1.1
Pancreas	2	2.32	0.9	1	4.36	0.2	7	2.80	2.5[b]	6	2.60	2.3	16	12.08	1.3
Respiratory system	**6**	**9.50**	**0.6**	**18**	**18.06**	**1.0**	**7**	**11.00**	**0.6**	**7**	**8.80**	**0.8**	**38**	**47.37**	**0.8**
Nasal cavities, sinuses	0	0.14	0.0	0	0.26	0.0	0	0.16	0.0	0	0.13	0.0	0	0.68	0.0
Larynx	0	0.61	0.0	1	1.16	0.9	0	0.70	0.0	0	0.54	0.0	1	3.01	0.3
Trachea, bronchus, lung	6	8.31	0.7	17	15.84	1.1	6	9.66	0.6	7	7.73	0.9	36	41.54	0.9
Female breast	5	5.15	1.0	7	9.56	0.7	6	6.26	1.0	9	6.22	1.4	27	27.18	1.0
Female genital tract	**7**	**4.78**	**1.5**	**7**	**8.78**	**0.8**	**6**	**5.47**	**1.1**	**1**	**4.98**	**0.2**	**21**	**24.00**	**0.9**
Cervix uteri	3	1.50	2.0	5	2.69	1.9	4	1.58	2.5	0	1.29	0.0	12	7.05	1.7
Corpus uteri	4	1.43	2.8	1	2.67	0.4	2	1.68	1.2	1	1.53	0.7	8	7.31	1.1
Uterus, NOS	0	0.10	0.0	0	0.16	0.0	0	0.11	0.0	0	0.12	0.0	0	0.49	0.0
Ovary, fallopian tubes	0	1.45	0.0	0	2.71	0.0	0	1.72	0.0	0	1.62	0.0	0	7.50	0.0[b]
Prostate gland	8	4.70	1.7	9	8.62	1.0	7	5.40	1.3	7	4.49	1.6	31	23.20	1.3
Testis	0	0.16	0.0	0	0.29	0.0	0	0.16	0.0	1	0.11	9.1	1	0.72	1.4
Kidney, renal pelvis, ureter	6	1.92	3.1[b]	2	3.57	0.6	4	2.23	1.8	1	1.95	0.5	13	9.67	1.3
Bladder, other urinary	27	3.81	7.1[b]	81	7.24	11.2[b]	23	4.53	5.1[b]	7	3.84	1.8	138	19.42	7.1[b]
Melanoma of the skin	1	0.67	1.5	1	1.28	0.8	0	0.80	0.0	0	0.69	0.0	2	3.45	0.6
Eye	1	0.19	5.3	1	0.34	2.9	0	0.20	0.0	0	0.17	0.0	2	0.90	2.2
Brain, central nervous system	4	1.19	3.4	2	2.20	0.9	1	1.30	0.8	2	1.03	1.9	9	5.73	1.6
Thyroid gland	0	0.28	0.0	0	0.51	0.0	2	0.33	6.1	1	0.32	3.1	3	1.43	2.1
Bone	0	0.11	0.0	0	0.19	0.0	0	0.12	0.0	0	0.10	0.0	0	0.51	0.0
Connective tissue	0	0.21	0.0	1	0.37	2.7	2	0.21	9.5[b]	0	0.18	0.0	3	0.97	3.1
Lymphatic, hematopoietic system	**3**	**3.76**	**0.8**	**10**	**6.96**	**1.4**	**4**	**4.36**	**0.9**	**6**	**3.89**	**1.5**	**23**	**18.97**	**1.2**
Non-Hodgkin's lymphoma	0	1.04	0.0	0	1.94	0.0	2	1.22	1.6	2	1.10	1.8	4	5.30	0.8
Hodgkin's disease	1	0.28	3.6	1	0.50	2.0	0	0.29	0.0	1	0.24	4.2	3	1.33	2.3
Multiple myeloma	1	0.72	1.4	2	1.35	1.5	0	0.85	0.0	1	0.77	1.3	4	3.68	1.1
Leukemias	1	1.68	0.6	6	3.10	1.9	2	1.94	1.0	2	1.75	1.1	11	8.47	1.3
Chronic lymphocytic	1	0.85	1.2	4	1.56	2.6	1	0.97	1.0	2	0.88	2.3	8	4.27	1.9
Acute nonlymphocytic	0	0.44	0.0	1	0.86	1.2	1	0.55	1.8	0	0.50	0.0	2	2.36	0.8

[a] ICD-7 code = 180.

[b] $P < .05$.

KIDNEY
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the kidney, renal pelvis, or ureter among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,122			2,686			1,041			461			5,122		
Person-yr in interval	3,693			6,438			3,544			2,450			16,126		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**46**	**37.03**	**1.2**	**118**	**67.14**	**1.8**[b]	**55**	**40.28**	**1.4**[b]	**36**	**31.21**	**1.2**	**255**	**175.65**	**1.5**[b]
All excluding site of initial cancer	**42**	**35.77**	**1.2**	**116**	**64.83**	**1.8**[b]	**51**	**38.90**	**1.3**	**35**	**30.15**	**1.2**	**244**	**169.64**	**1.4**[b]
Buccal cavity, pharynx	**2**	**1.21**	**1.7**	**0**	**2.13**	**0.0**	**0**	**1.23**	**0.0**	**0**	**0.90**	**0.0**	**2**	**5.47**	**0.4**
Lip	1	0.65	1.5	0	1.14	0.0	0	0.65	0.0	0	0.47	0.0	1	2.92	0.3
Tongue	0	0.09	0.0	0	0.16	0.0	0	0.09	0.0	0	0.07	0.0	0	0.40	0.0
Salivary gland	0	0.10	0.0	0	0.17	0.0	0	0.10	0.0	0	0.07	0.0	0	0.44	0.0
Gum, other mouth	0	0.17	0.0	0	0.31	0.0	0	0.18	0.0	0	0.14	0.0	0	0.80	0.0
Pharynx	1	0.20	5.1	0	0.35	0.0	0	0.21	0.0	0	0.15	0.0	1	0.91	1.1
Digestive system	**5**	**13.29**	**0.4**[b]	**24**	**23.18**	**1.0**	**12**	**13.79**	**0.9**	**14**	**10.68**	**1.3**	**55**	**60.94**	**0.9**
Esophagus	0	0.59	0.0	0	1.00	0.0	0	0.59	0.0	0	0.44	0.0	0	2.61	0.0
Stomach	2	4.00	0.5	7	6.56	1.1	2	3.79	0.5	0	2.86	0.0	11	17.21	0.6
Colon	0	3.06	0.0	9	5.53	1.6	3	3.38	0.9	6	2.72	2.2	18	14.68	1.2
Rectum	3	3.01	1.0	5	5.25	1.0	3	3.11	1.0	1	2.38	0.4	12	13.75	0.9
Liver, biliary	0	0.76	0.0	3	1.43	2.1	0	0.88	0.0	1	0.70	1.4	4	3.77	1.1
Pancreas	0	1.46	0.0	0	2.70	0.0	4	1.63	2.5	4	1.27	3.1	8	7.06	1.1
Respiratory system	**4**	**8.20**	**0.5**	**13**	**15.53**	**0.8**	**7**	**9.28**	**0.8**	**4**	**7.01**	**0.6**	**28**	**40.02**	**0.7**
Nasal cavities, sinuses	0	0.10	0.0	0	0.19	0.0	0	0.11	0.0	0	0.08	0.0	0	0.48	0.0
Larynx	0	0.56	0.0	1	1.06	0.9	0	0.63	0.0	0	0.47	0.0	1	2.72	0.4
Trachea, bronchus, lung	4	7.20	0.6	12	13.68	0.9	6	8.18	0.7	4	6.19	0.6	26	35.25	0.7
Prostate gland	8	4.70	1.7	9	8.62	1.0	7	5.40	1.3	7	4.49	1.6	31	23.20	1.3
Testis	0	0.16	0.0	0	0.29	0.0	0	0.16	0.0	1	0.11	9.1	1	0.72	1.4
Kidney, renal pelvis, ureter	4	1.26	3.2	2	2.31	0.9	4	1.38	2.9	1	1.06	0.9	11	6.01	1.8
Bladder, other urinary	18	3.12	5.8[b]	59	5.91	10.0[b]	18	3.60	5.0[b]	3	2.82	1.1	98	15.45	6.3[b]
Melanoma of the skin	1	0.34	2.9	1	0.64	1.6	0	0.38	0.0	0	0.28	0.0	2	1.65	1.2
Eye	1	0.12	8.4	1	0.21	4.8	0	0.12	0.0	0	0.09	0.0	2	0.54	3.7
Brain, central nervous system	1	0.70	1.4	1	1.28	0.8	0	0.72	0.0	1	0.50	2.0	3	3.20	0.9
Thyroid gland	0	0.11	0.0	0	0.20	0.0	1	0.12	8.6	0	0.09	0.0	1	0.51	2.0
Bone	0	0.07	0.0	0	0.12	0.0	0	0.07	0.0	0	0.05	0.0	0	0.30	0.0
Connective tissue	0	0.13	0.0	1	0.22	4.6	2	0.12	16.1[b]	0	0.09	0.0	3	0.56	5.3[b]
Lymphatic, hematopoietic system	**2**	**2.45**	**0.8**	**5**	**4.46**	**1.1**	**3**	**2.66**	**1.1**	**4**	**2.05**	**1.9**	**14**	**11.62**	**1.2**
Non-Hodgkin's lymphoma	0	0.65	0.0	0	1.19	0.0	1	0.71	1.4	2	0.54	3.7	3	3.09	1.0
Hodgkin's disease	1	0.19	5.3	1	0.33	3.0	0	0.18	0.0	1	0.13	7.4	3	0.84	3.6
Multiple myeloma	1	0.46	2.2	1	0.84	1.2	0	0.50	0.0	1	0.39	2.6	3	2.18	1.4
Leukemias	0	1.13	0.0	2	2.06	1.0	2	1.23	1.6	0	0.97	0.0	4	5.39	0.7
Chronic lymphocytic	0	0.61	0.0	1	1.11	0.9	1	0.66	1.5	0	0.52	0.0	2	2.91	0.7
Acute nonlymphocytic	0	0.28	0.0	1	0.54	1.8	1	0.33	3.0	0	0.26	0.0	2	1 42	1.4

[a] ICD-7 code = 180.

[b] $P < .05$.

KIDNEY
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the kidney, renal pelvis, or ureter among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,040			2,155			892			451			4,040		
Person-yr in interval	2,937			5,267			3,214			2,828			14,246		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**32**	**24.53**	**1.3**	**63**	**45.62**	**1.4^b**	**31**	**30.47**	**1.0**	**35**	**31.59**	**1.1**	**161**	**132.20**	**1.2^b**
All excluding site of initial cancer	**30**	**23.87**	**1.3**	**63**	**44.36**	**1.4^b**	**31**	**29.62**	**1.0**	**35**	**30.70**	**1.1**	**159**	**128.54**	**1.2^b**
Buccal cavity, pharynx	**0**	**0.33**	**0.0**	**1**	**0.61**	**1.7**	**0**	**0.41**	**0.0**	**0**	**0.44**	**0.0**	**1**	**1.78**	**0.6**
Lip	0	0.05	0.0	0	0.09	0.0	0	0.06	0.0	0	0.07	0.0	0	0.28	0.0
Tongue	0	0.06	0.0	0	0.10	0.0	0	0.07	0.0	0	0.08	0.0	0	0.31	0.0
Salivary gland	0	0.07	0.0	0	0.13	0.0	0	0.08	0.0	0	0.08	0.0	0	0.36	0.0
Gum, other mouth	0	0.09	0.0	0	0.17	0.0	0	0.12	0.0	0	0.15	0.0	0	0.53	0.0
Pharynx	0	0.06	0.0	1	0.11	9.0	0	0.07	0.0	0	0.07	0.0	1	0.31	3.2
Digestive system	**3**	**8.25**	**0.4**	**13**	**15.25**	**0.9**	**11**	**10.61**	**1.0**	**14**	**11.78**	**1.2**	**41**	**45.88**	**0.9**
Esophagus	0	0.22	0.0	1	0.40	2.5	0	0.29	0.0	0	0.33	0.0	1	1.25	0.8
Stomach	0	2.04	0.0	1	3.54	0.3	0	2.45	0.0	2	2.64	0.8	3	10.66	0.3^b
Colon	0	2.58	0.0	5	4.90	1.0	5	3.46	1.4	6	3.95	1.5	16	14.89	1.1
Rectum	1	1.49	0.7	2	2.75	0.7	1	1.86	0.5	2	1.98	1.0	6	8.07	0.7
Liver, biliary	0	0.72	0.0	2	1.40	1.4	1	0.99	1.0	2	1.14	1.8	5	4.25	1.2
Pancreas	2	0.86	2.3	1	1.66	0.6	3	1.17	2.6	2	1.33	1.5	8	5.02	1.6
Respiratory system	**2**	**1.30**	**1.5**	**5**	**2.53**	**2.0**	**0**	**1.72**	**0.0**	**3**	**1.79**	**1.7**	**10**	**7.35**	**1.4**
Nasal cavities, sinuses	0	0.04	0.0	0	0.07	0.0	0	0.05	0.0	0	0.05	0.0	0	0.20	0.0
Larynx	0	0.05	0.0	0	0.10	0.0	0	0.07	0.0	0	0.07	0.0	0	0.29	0.0
Trachea, bronchus, lung	2	1.11	1.8	5	2.16	2.3	0	1.48	0.0	3	1.54	1.9	10	6.29	1.6
Female breast	5	5.15	1.0	7	9.56	0.7	6	6.26	1.0	9	6.22	1.4	27	27.18	1.0
Female genital tract	**7**	**4.78**	**1.5**	**7**	**8.78**	**0.8**	**6**	**5.47**	**1.1**	**1**	**4.98**	**0.2**	**21**	**24.00**	**0.9**
Cervix uteri	3	1.50	2.0	5	2.69	1.9	4	1.58	2.5	0	1.29	0.0	12	7.05	1.7
Corpus uteri	4	1.43	2.8	1	2.67	0.4	2	1.68	1.2	1	1.53	0.7	8	7.31	1.1
Uterus, NOS	0	0.10	0.0	0	0.16	0.0	0	0.11	0.0	0	0.12	0.0	0	0.49	0.0
Ovary, fallopian tubes	0	1.45	0.0	0	2.71	0.0	0	1.72	0.0	0	1.62	0.0	0	7.50	0.0^b
Kidney, renal pelvis, ureter	2	0.66	3.0	0	1.26	0.0	0	0.85	0.0	0	0.89	0.0	2	3.66	0.5
Bladder, other urinary	9	0.69	13.1^b	22	1.33	16.5^b	5	0.93	5.4^b	4	1.02	3.9^b	40	3.97	10.1^b
Melanoma of the skin	0	0.33	0.0	0	0.64	0.0	0	0.42	0.0	0	0.41	0.0	0	1.80	0.0
Eye	0	0.07	0.0	0	0.13	0.0	0	0.08	0.0	0	0.08	0.0	0	0.36	0.0
Brain, central nervous system	3	0.49	6.1^b	1	0.92	1.1	1	0.58	1.7	1	0.53	1.9	6	2.53	2.4
Thyroid gland	0	0.17	0.0	0	0.31	0.0	1	0.21	4.7	1	0.23	4.4	2	0.92	2.2
Bone	0	0.04	0.0	0	0.07	0.0	0	0.05	0.0	0	0.05	0.0	0	0.21	0.0
Connective tissue	0	0.08	0.0	0	0.15	0.0	0	0.09	0.0	0	0.09	0.0	0	0.41	0.0
Lymphatic, hematopoietic system	**1**	**1.31**	**0.8**	**5**	**2.50**	**2.0**	**1**	**1.70**	**0.6**	**2**	**1.84**	**1.1**	**9**	**7.35**	**1.2**
Non-Hodgkin's lymphoma	0	0.39	0.0	0	0.75	0.0	1	0.51	1.9	0	0.56	0.0	1	2.21	0.5
Hodgkin's disease	0	0.09	0.0	0	0.17	0.0	0	0.11	0.0	0	0.11	0.0	0	0.49	0.0
Multiple myeloma	0	0.26	0.0	1	0.51	2.0	0	0.35	0.0	0	0.38	0.0	1	1.50	0.7
Leukemias	1	0.55	1.8	4	1.04	3.8^b	0	0.71	0.0	2	0.78	2.6	7	3.08	2.3
Chronic lymphocytic	1	0.24	4.2	3	0.45	6.7^b	0	0.31	0.0	2	0.36	5.6	6	1.36	4.4^b
Acute nonlymphocytic	0	0.16	0.0	0	0.32	0.0	0	0.22	0.0	0	0.24	0.0	0	0.94	0.0

[a] ICD-7 code = 180.

[b] $P < .05$.

BLADDER
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the bladder or other urinary (including papillomas), 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	15,236	4,730	19,966
No. who developed a second primary cancer	1,163	260	1,423
Average age at diagnosis of first cancer, yr	66	67	66
Average yr of diagnosis of first cancer	1968	1967	1968
Person-yr of follow-up	72,216	22,583	94,799
Average follow-up, yr	4.7	4.8	4.7
Percent given radiotherapy for first cancer	34	34	34

[a] ICD-7 code = 181.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the bladder or other urinary (including papillomas) in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	1,143	80.3
Only the first cancer	147	10.3
Only the second cancer	105	7.4
Neither first nor second cancer	28	2.0
Total second primary cancers	1,423	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

BLADDER
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bladder or other urinary (including papillomas) among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval		19,966			13,973			6,539			3,055			19,966	
Person-yr in interval		16,765			37,347			22,808			17,879			94,799	
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**199**	**203.60**	**1.0**	**579**	**462.90**	**1.3**[b]	**342**	**302.91**	**1.1**[b]	**303**	**269.89**	**1.1**	**1,423**	**1,239.30**	**1.1**[b]
All excluding site of initial cancer	**175**	**188.22**	**0.9**	**522**	**427.12**	**1.2**[b]	**304**	**279.55**	**1.1**	**277**	**248.93**	**1.1**	**1,278**	**1,143.81**	**1.1**[b]
Buccal cavity, pharynx	**4**	**5.54**	**0.7**	**17**	**12.43**	**1.4**	**8**	**7.85**	**1.0**	**7**	**6.66**	**1.1**	**36**	**32.48**	**1.1**
Lip	3	2.77	1.1	7	6.22	1.1	3	3.86	0.8	2	3.19	0.6	15	16.05	0.9
Tongue	0	0.46	0.0	1	1.02	1.0	2	0.66	3.0	0	0.56	0.0	3	2.70	1.1
Salivary gland	1	0.51	2.0	1	1.14	0.9	0	0.72	0.0	2	0.59	3.4	4	2.96	1.4
Gum, other mouth	0	0.89	0.0	5	2.05	2.4	0	1.35	0.0	1	1.25	0.8	6	5.53	1.1
Pharynx	0	0.89	0.0	3	2.01	1.5	3	1.26	2.4	2	1.07	1.9	8	5.23	1.5
Digestive system	**38**	**73.10**	**0.5**[b]	**139**	**163.04**	**0.9**	**96**	**107.01**	**0.9**	**72**	**95.77**	**0.8**[b]	**345**	**438.93**	**0.8**[b]
Esophagus	2	2.93	0.7	2	6.41	0.3	3	4.10	0.7	4	3.55	1.1	11	16.98	0.6
Stomach	10	20.73	0.5[b]	33	44.60	0.7	18	28.56	0.6[b]	13	24.33	0.5[b]	74	118.22	0.6[b]
Colon	10	18.57	0.5[b]	36	42.27	0.9	30	28.50	1.1	20	26.73	0.7	96	116.06	0.8
Rectum	8	15.63	0.5	32	34.91	0.9	16	22.65	0.7	16	19.84	0.8	72	93.03	0.8[b]
Liver, biliary	2	4.82	0.4	12	11.14	1.1	13	7.56	1.7	7	7.15	1.0	34	30.67	1.1
Pancreas	5	8.09	0.6	20	18.64	1.1	15	12.40	1.2	11	11.31	1.0	51	50.45	1.0
Respiratory system	**43**	**37.96**	**1.1**	**154**	**88.69**	**1.7**[b]	**92**	**56.73**	**1.6**[b]	**82**	**49.00**	**1.7**[b]	**371**	**232.42**	**1.6**[b]
Nasal cavities, sinuses	0	0.51	0.0	2	1.14	1.8	2	0.72	2.8	1	0.62	1.6	5	2.98	1.7
Larynx	2	2.47	0.8	13	5.73	2.3[b]	2	3.61	0.6	5	3.05	1.6	22	14.85	1.5
Trachea, bronchus, lung	39	33.32	1.2	136	78.07	1.7[b]	82	50.01	1.6[b]	72	43.22	1.7[b]	329	204.61	1.6[b]
Female breast	7	7.89	0.9	17	17.56	1.0	8	12.23	0.7	10	11.83	0.8	42	49.52	0.8
Female genital tract	**4**	**6.76**	**0.6**	**16**	**14.97**	**1.1**	**7**	**10.00**	**0.7**	**9**	**8.99**	**1.0**	**36**	**40.73**	**0.9**
Cervix uteri	2	1.95	1.0	7	4.23	1.7	2	2.68	0.7	4	2.19	1.8	15	11.05	1.4
Corpus uteri	1	2.04	0.5	3	4.57	0.7	1	3.06	0.3	0	2.76	0.0	5	12.42	0.4[b]
Uterus, NOS	1	0.16	6.1	1	0.34	3.0	0	0.24	0.0	0	0.23	0.0	2	0.97	2.1
Ovary, fallopian tubes	0	2.12	0.0	4	4.73	0.8	2	3.22	0.6	4	2.98	1.3	10	13.06	0.8
Prostate gland	37	22.80	1.6[b]	62	52.58	1.2	38	34.95	1.1	42	31.93	1.3	79	142.26	1.3[b]
Testis	1	0.53	1.9	2	1.20	1.7	2	0.73	2.8	0	0.54	0.0	5	2.99	1.7
Kidney, renal pelvis, ureter	24	6.54	3.7[b]	58	15.01	3.9[b]	26	9.82	2.6[b]	20	8.69	2.3[b]	128	40.05	3.2[b]
Bladder, other urinary	24	15.38	1.6	57	35.78	1.6[b]	38	23.36	1.6[b]	26	20.96	1.2	145	95.49	1.5[b]
Melanoma of the skin	2	1.88	1.1	5	4.36	1.1	0	2.81	0.0	1	2.48	0.4	8	11.53	0.7
Eye	1	0.60	1.7	1	1.33	0.8	0	0.84	0.0	0	0.71	0.0	2	3.47	0.6
Brain, central nervous system	1	3.36	0.3	6	7.68	0.8	3	4.79	0.6	1	3.91	0.3	11	19.74	0.6[b]
Thyroid gland	1	0.73	1.4	1	1.67	0.6	0	1.11	0.0	3	1.00	3.0	5	4.53	1.1
Bone	0	0.33	0.0	0	0.75	0.0	1	0.47	2.1	2	0.39	5.1	3	1.94	1.5
Connective tissue	0	0.64	0.0	3	1.40	2.1	0	0.88	0.0	1	0.74	1.4	4	3.67	1.1
Lymphatic, hematopoietic system	**9**	**12.84**	**0.7**	**34**	**29.43**	**1.2**	**18**	**19.32**	**0.9**	**18**	**17.22**	**1.0**	**79**	**78.82**	**1.0**
Non-Hodgkin's lymphoma	1	3.44	0.3	11	7.93	1.4	5	5.20	1.0	8	4.64	1.7	25	21.20	1.2
Hodgkin's disease	1	0.86	1.2	3	1.94	1.5	2	1.22	1.6	2	1.00	2.0	8	5.01	1.6
Multiple myeloma	1	2.48	0.4	5	5.69	0.9	3	3.76	0.8	2	3.36	0.6	11	15.29	0.7
Leukemias	6	5.95	1.0	15	13.59	1.1	7	8.96	0.8	6	8.05	0.7	34	36.54	0.9
Chronic lymphocytic	2	3.19	0.6	8	7.26	1.1	2	4.80	0.4	4	4.32	0.9	16	19.58	0.8
Acute nonlymphocytic	4	1.54	2.6	7	3.63	1.9	3	2.42	1.2	0	2.22	0.0	14	9.81	1.4

[a] ICD-7 code = 181.

[b] $P < .05$.

BLADDER
MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bladder or other urinary (including papillomas) among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	15,236			10,826			5,034			2,281			15,236		
Person-yr in interval	12,913			28,914			17,279			13,110			72,216		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**167**	**164.39**	**1.0**	**470**	**376.01**	**1.2**[b]	**282**	**241.32**	**1.2**[b]	**244**	**208.94**	**1.2**[b]	**1,163**	**990.66**	**1.2**[b]
All excluding site of initial cancer	**146**	**150.19**	**1.0**	**421**	**342.90**	**1.2**[b]	**252**	**219.90**	**1.1**[b]	**223**	**190.01**	**1.2**[b]	**1,042**	**902.99**	**1.2**[b]
Buccal cavity, pharynx	**4**	**5.00**	**0.8**	**15**	**11.24**	**1.3**	**6**	**7.00**	**0.9**	**4**	**5.80**	**0.7**	**29**	**29.04**	**1.0**
Lip	3	2.69	1.1	6	6.03	1.0	2	3.73	0.5	2	3.05	0.7	13	15.51	0.8
Tongue	0	0.36	0.0	0	0.81	0.0	1	0.51	2.0	0	0.41	0.0	1	2.09	0.5
Salivary gland	1	0.40	2.5	1	0.91	1.1	0	0.57	0.0	1	0.46	2.2	3	2.35	1.3
Gum, other mouth	0	0.73	0.0	5	1.68	3.0	0	1.07	0.0	0	0.94	0.0	5	4.42	1.1
Pharynx	0	0.80	0.0	3	1.81	1.7	3	1.12	2.7	1	0.94	1.1	7	4.67	1.5
Digestive system	**33**	**58.87**	**0.6**[b]	**105**	**131.85**	**0.8**[b]	**76**	**84.23**	**0.9**	**58**	**72.35**	**0.8**	**272**	**347.31**	**0.8**[b]
Esophagus	2	2.53	0.8	2	5.54	0.4	3	3.45	0.9	4	2.87	1.4	11	14.39	0.8
Stomach	9	17.18	0.5[b]	24	37.26	0.6[b]	13	23.31	0.6[b]	12	19.22	0.6	58	96.96	0.6[b]
Colon	9	14.07	0.6	25	32.13	0.8	22	20.99	1.0	12	18.76	0.6	68	85.95	0.8
Rectum	6	13.18	0.5[b]	28	29.54	0.9	15	18.78	0.8	16	15.98	1.0	65	77.48	0.8
Liver, biliary	2	3.54	0.6	7	8.24	0.8	10	5.39	1.9	6	4.82	1.2	25	21.99	1.1
Pancreas	5	6.60	0.8	15	15.24	1.0	12	9.89	1.2	8	8.62	0.9	40	40.36	1.0
Respiratory system	**41**	**35.85**	**1.1**	**144**	**83.87**	**1.7**[b]	**89**	**53.37**	**1.7**[b]	**76**	**45.54**	**1.7**[b]	**350**	**218.62**	**1.6**[b]
Nasal cavities, sinuses	0	0.45	0.0	2	1.01	2.0	2	0.63	3.2	1	0.53	1.9	5	2.61	1.9
Larynx	1	2.39	0.4	13	5.54	2.3[b]	2	3.48	0.6	5	2.93	1.7	21	14.33	1.5
Trachea, bronchus, lung	38	31.53	1.2	126	73.95	1.7[b]	80	47.09	1.7[b]	67	40.25	1.7[b]	311	192.82	1.6[b]
Prostate gland	37	22.80	1.6[b]	62	52.58	1.2	38	34.95	1.1	42	31.93	1.3	179	142.26	1.3[b]
Testis	1	0.53	1.9	2	1.20	1.7	2	0.73	2.8	0	0.54	0.0	5	2.99	1.7
Kidney, renal pelvis, ureter	16	5.47	2.9[b]	48	12.61	3.8[b]	20	8.11	2.5[b]	13	6.97	1.9	97	33.16	2.9[b]
Bladder, other urinary	21	14.20	1.5	49	33.11	1.5[b]	30	21.42	1.4	21	18.93	1.1	121	87.67	1.4[b]
Melanoma of the skin	1	1.38	0.7	4	3.21	1.2	0	2.02	0.0	1	1.72	0.6	6	8.33	0.7
Eye	1	0.49	2.1	1	1.10	0.9	0	0.68	0.0	0	0.56	0.0	2	2.83	0.7
Brain, central nervous system	1	2.67	0.4	4	6.12	0.7	3	3.75	0.8	1	2.96	0.3	9	15.49	0.6
Thyroid gland	1	0.46	2.2	0	1.06	0.0	0	0.67	0.0	2	0.55	3.6	3	2.75	1.1
Bone	0	0.27	0.0	0	0.61	0.0	1	0.38	2.6	2	0.30	6.8	3	1.56	1.9
Connective tissue	0	0.52	0.0	3	1.14	2.6	0	0.70	0.0	0	0.58	0.0	3	2.94	1.0
Lymphatic, hematopoietic system	**7**	**10.69**	**0.7**	**26**	**24.57**	**1.1**	**14**	**15.80**	**0.9**	**16**	**13.61**	**1.2**	**63**	**64.68**	**1.0**
Non-Hodgkin's lymphoma	1	2.79	0.4	8	6.46	1.2	3	4.14	0.7	7	3.54	2.0	19	16.93	1.1
Hodgkin's disease	0	0.72	0.0	3	1.63	1.8	2	1.01	2.0	2	0.80	2.5	7	4.15	1.7
Multiple myeloma	1	2.04	0.5	4	4.69	0.9	2	3.03	0.7	2	2.62	0.8	9	12.38	0.7
Leukemias	5	5.04	1.0	11	11.54	1.0	6	7.47	0.8	5	6.51	0.8	27	30.56	0.9
Chronic lymphocytic	2	2.78	0.7	6	6.34	0.9	1	4.11	0.2	4	3.60	1.1	13	16.84	0.8
Acute nonlymphocytic	3	1.27	2.4	5	3.01	1.7	3	1.97	1.5	0	1.75	0.0	11	8.00	1.4

[a] ICD-7 code = 181.

[b] $P < .05$.

BLADDER
FEMALES

TABLE 2E. —*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bladder or other urinary (including papillomas) among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,730			3,147			1,505			774			4,730		
Person-yr in interval	3,851			8,433			5,529			4,769			22,583		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**32**	**39.21**	**0.8**	**109**	**86.89**	**1.3**[b]	**60**	**61.59**	**1.0**	**59**	**60.95**	**1.0**	**260**	**248.64**	**1.0**
All excluding site of initial cancer	**29**	**38.03**	**0.8**	**101**	**84.22**	**1.2**	**52**	**59.65**	**0.9**	**54**	**58.92**	**0.9**	**236**	**240.82**	**1.0**
Buccal cavity, pharynx	**0**	**0.54**	**0.0**	**2**	**1.19**	**1.7**	**2**	**0.85**	**2.3**	**3**	**0.86**	**3.5**	**7**	**3.44**	**2.0**
Lip	0	0.08	0.0	1	0.19	5.4	1	0.13	7.4	0	0.14	0.0	2	0.54	3.7
Tongue	0	0.10	0.0	1	0.21	4.8	1	0.15	6.6	0	0.15	0.0	2	0.61	3.3
Salivary gland	0	0.11	0.0	0	0.23	0.0	0	0.15	0.0	1	0.13	7.7	1	0.61	1.6
Gum, other mouth	0	0.16	0.0	0	0.37	0.0	0	0.28	0.0	1	0.31	3.2	1	1.11	0.9
Pharynx	0	0.09	0.0	0	0.20	0.0	0	0.14	0.0	1	0.13	7.7	1	0.56	1.8
Digestive system	**5**	**14.23**	**0.4**[b]	**34**	**31.19**	**1.1**	**20**	**22.78**	**0.9**	**14**	**23.42**	**0.6**	**73**	**91.62**	**0.8**
Esophagus	0	0.40	0.0	0	0.87	0.0	0	0.65	0.0	0	0.68	0.0	0	2.59	0.0
Stomach	1	3.55	0.3	9	7.34	1.2	5	5.25	1.0	1	5.11	0.2	16	21.26	0.8
Colon	1	4.50	0.2	11	10.14	1.1	8	7.51	1.1	8	7.97	1.0	28	30.11	0.9
Rectum	2	2.45	0.8	4	5.37	0.7	1	3.87	0.3	0	3.86	0.0[b]	7	15.55	0.5[b]
Liver, biliary	0	1.28	0.0	5	2.90	1.7	3	2.17	1.4	1	2.33	0.4	9	8.68	1.0
Pancreas	0	1.49	0.0	5	3.40	1.5	3	2.51	1.2	3	2.69	1.1	11	10.09	1.1
Respiratory system	**2**	**2.11**	**0.9**	**10**	**4.82**	**2.1**	**3**	**3.41**	**0.9**	**6**	**3.46**	**1.7**	**21**	**13.80**	**1.5**
Nasal cavities, sinuses	0	0.06	0.0	0	0.13	0.0	0	0.09	0.0	0	0.09	0.0	0	0.37	0.0
Larynx	1	0.08	12.0	0	0.19	0.0	0	0.13	0.0	0	0.12	0.0	1	0.52	1.9
Trachea, bronchus, lung	1	1.79	0.6	10	4.12	2.4[b]	2	2.92	0.7	5	2.97	1.7	18	11.79	1.5
Female breast	7	7.89	0.9	17	17.56	1.0	8	12.23	0.7	10	11.83	0.8	42	49.52	0.8
Female genital tract	**4**	**6.76**	**0.6**	**16**	**14.97**	**1.1**	**7**	**10.00**	**0.7**	**9**	**8.99**	**1.0**	**36**	**40.73**	**0.9**
Cervix uteri	2	1.95	1.0	7	4.23	1.7	2	2.68	0.7	4	2.19	1.8	15	11.05	1.4
Corpus uteri	1	2.04	0.5	3	4.57	0.7	1	3.06	0.3	0	2.76	0.0	5	12.42	0.4[b]
Uterus, NOS	1	0.16	6.1	1	0.34	3.0	0	0.24	0.0	0	0.23	0.0	2	0.97	2.1
Ovary, fallopian tubes	0	2.12	0.0	4	4.73	0.8	2	3.22	0.6	4	2.98	1.3	10	13.06	0.8
Kidney, renal pelvis, ureter	8	1.07	7.5[b]	10	2.40	4.2[b]	6	1.71	3.5[b]	7	1.72	4.1[b]	31	6.89	4.5[b]
Bladder, other urinary	3	1.18	2.5	8	2.67	3.0[b]	8	1.94	4.1[b]	5	2.03	2.5	24	7.82	3.1[b]
Melanoma of the skin	1	0.50	2.0	1	1.15	0.9	0	0.79	0.0	0	0.76	0.0	2	3.20	0.6
Eye	0	0.11	0.0	0	0.23	0.0	0	0.16	0.0	0	0.15	0.0	0	0.64	0.0
Brain, central nervous system	0	0.69	0.0	2	1.56	1.3	0	1.04	0.0	0	0.95	0.0	2	4.25	0.5
Thyroid gland	0	0.27	0.0	1	0.61	1.6	0	0.44	0.0	1	0.45	2.2	2	1.78	1.1
Bone	0	0.06	0.0	0	0.14	0.0	0	0.09	0.0	0	0.09	0.0	0	0.38	0.0
Connective tissue	0	0.12	0.0	0	0.26	0.0	0	0.18	0.0	1	0.16	6.1	1	0.73	1.4
Lymphatic, hematopoietic system	**2**	**2.15**	**0.9**	**8**	**4.86**	**1.6**	**4**	**3.52**	**1.1**	**2**	**3.61**	**0.6**	**16**	**14.14**	**1.1**
Non-Hodgkin's lymphoma	0	0.65	0.0	3	1.47	2.0	2	1.06	1.9	1	1.10	0.9	6	4.27	1.4
Hodgkin's disease	1	0.14	7.1	0	0.31	0.0	0	0.21	0.0	0	0.20	0.0	1	0.86	1.2
Multiple myeloma	0	0.44	0.0	1	1.00	1.0	1	0.73	1.4	0	0.74	0.0	2	2.91	0.7
Leukemias	1	0.91	1.1	4	2.05	2.0	1	1.49	0.7	1	1.54	0.6	7	5.98	1.2
Chronic lymphocytic	0	0.41	0.0	2	0.92	2.2	1	0.69	1.5	0	0.72	0.0	3	2.74	1.1
Acute nonlymphocytic	1	0.27	3.8	2	0.62	3.2	0	0.45	0.0	0	0.47	0.0	3	1.81	1.7

[a] ICD-7 code = 181.

[b] $P < .05$.

Second Cancer Following Cutaneous Melanoma and Cancers of the Brain, Thyroid, Connective Tissue, Bone, and Eye in Denmark, 1943–80 [1]

Anne Østerlind, Jørgen H. Olsen, Elsebeth Lynge, *and* Marianne Ewertz [2]

ABSTRACT—Second primary cancers were studied in persons with rare tumors between 1943 and 1980. The risk of developing a new cancer was evaluated in 7,211 persons with cutaneous melanoma, 1,784 persons with eye cancer, 10,273 persons with tumors of the brain and nervous system, 1,935 persons with thyroid cancer, 1,542 persons with bone tumors, and 2,318 persons with malignant neoplasms of the connective tissue. All cancer patients were diagnosed in Denmark between 1943 and 1980 and survived for 2 or more months. Nonmelanoma skin cancers were excluded from the analysis, whereas tumors of the brain and nervous system included both benign and malignant neoplasms. Overall, patients with these cancers showed no greater incidence of new tumors than expected from comparisons with the general population. An excess of chronic lymphocytic leukemia was observed subsequent to all cancers derived from the neural tube, i.e., melanoma and tumors of the eye, brain, and nervous system. Bone cancer occurred excessively, although the possibility of misclassified metastases could not be eliminated. Patients with tumors of the brain and nervous system who survived for 10 or more years developed significantly more cancers of the kidney and connective tissue and melanoma than anticipated. A deficit of second cancers of the digestive system was noted after primary bone and connective tissue cancers, in contrast to an excess of second cancers of the lung and kidney. Although based on few cases, patients with bone cancer showed a large excess of eye cancer as a second primary. The association between cancers of the breast and connective tissue was found to be bidirectional. Persons with connective tissue cancer were at increased risk of developing non-Hodgkin's lymphoma. Thyroid cancer patients were at high risk of subsequent tumors of the brain and nervous tissue and non-Hodgkin's lymphoma. However, contrary to previous reports, the risk of breast cancer was not elevated following thyroid cancer.—Natl Cancer Inst Monogr 68: 361-388, 1985.

MALIGNANT MELANOMA (ICD-7, 190)

Malignant melanoma of the skin represents 1.6% of all cancers in men and 2.5% in women. Between 1943 and 1980, the increase in the incidence rate for both sexes was fivefold to sixfold. The increase was most pronounced after 1962, and at present we see no indication that this increase is equalizing. A similar increase has not been observed for any other cancer in Denmark in recent years. In 1978–80, the age-standardized incidence rate was 6.1/100,000 man-years and 8.5/100,000 woman-years (*1, 2*).

Solar UV light seems to play an important part in the causation of malignant melanoma of the skin; the mode of action is not entirely clear. Other risk factors include race, skin pigmentation, genetic susceptibility, high social class, and possibly hormonal factors (*3, 4*). The prognosis after diagnosis of malignant melanoma is favorable, particularly among women. In Norway, the 5-year relative survival rates were 59% in men and 78% in women in 1968–75 (*5*).

Results

Our present records include data on 7,211 persons who survived for 2 or more months after a diagnosis of malignant melanoma of the skin between 1943 and 1980. Slightly more than 60% were women. The average age at diagnosis was 53 years, and the average follow-up was 4.8 years for men and 6.7 years for women. The initial treatment involved surgery 90% and radiation therapy 15% of the time.

Overall, 312 (or 4.3%) patients developed a second cancer (RR= 1.01; 95% CI = 0.90–1.13). The Registry rarely includes more than 1 tumor of a given site, and 4 new melanomas of the skin were disregarded for this reason. The risk of developing a second cancer did not vary by time after initial diagnosis, and no sites were significantly above or below expectation. An increased risk of bone cancer in men was based only on 2 cases, whereas no bone cancers occurred in women. A slight excess of endometrial cancer was observed among women (RR = 1.5; 95% CI= 0.9–2.4), and a small excess of CLL was seen among men (RR = 2.8; 95% CI= 0.9–6.4). There were 2 cancers of the eye, including intraocular melanoma, against 0.88 cases expected. The risk for cancer of the female breast (RR = 1.1) was not significantly increased.

Discussion

Persons diagnosed with maligant melanoma of the skin were at no greater risk of developing a new cancer than were individuals in the general population. The absence of a risk of second melanomas is in line with the Registry's practice of not accepting second tumors of the same site. Metastatic spread to the bone may have accounted for the occurrence of 2 such tumors in men. Possibly because of immunologic defects common to both diseases (*6*), CLL has been associated with melanoma. The suggestive risk of

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ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; RR = relative risk(s); CI = confidence interval; CLL = chronic lymphocytic leukemia; NHL = non-Hodgkin's lymphoma.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Anne Østerlind, M.D.

CLL observed in our study is in accord with these previous findings, although the numbers are small and the risk was seen only in males. An increased risk of breast cancer subsequent to malignant melanoma has been reported (*7*) but was not found in the current analysis. The suggestive risk of uterine cancer following malignant melanoma is worth attention in view of the possibility that exogenous estrogens may contribute to the risk of both diseases (*8*).

EYE (ICD-7, 192)

Cancer of the eye accounts for only 0.3% of all cancers in Denmark (*1*). The rates are slightly higher among males than females. Between 1962 and 1972, the 5-year survival rate was approximately 71% (*9*). Eye cancer includes a variety of tumors, such as intraocular melanoma, retinoblastoma, and orbital and lacrimal gland cancers. Retinoblastoma, a disease of childhood, accounts for about 6% of all eye cancers and occurs usually before the child is 15 years old. Most eye cancers appear in later life and are predominantly intraocular melanomas (*10*). Bilateral cases of retinoblastoma are assumed to be hereditary (*11, 12*). Previous studies (*13, 14*) revealed a link between retinoblastoma and second cancers, primarily osteosarcomas occurring in bones, both inside and at a distance from radiation treatment fields.

Results

Between 1943 and 1980, the Registry was notified of 1,784 persons who survived 2 or more months after a diagnosis of eye cancer. The average age at diagnosis was 54 years, and the average follow-up was 8.2 years in both men and women. The average year of diagnosis was 1963. Radiation was given as part of the treatment to 14% of the patients. A total of 119 patients (or 6.7%) developed a second cancer compared with 118.4 expected from the rates in the general population (RR = 1.00; 95% CI = 0.83–1.20). The risk of all types of cancer increased with time, though the trend was not significant ($P = .06$).

Cancer of the digestive organs accounted for 46% of all new cancers, 51% among males (RR = 1.4; 95% CI = 1.0–2.0) and 38% among females (RR = 1.1; 95% CI = 0.6–1.7). Only cancers of the liver and gallbladder were significantly elevated (RR = 3.0; 95% CI = 1.4–5.8); however, there was no evidence for increasing risks over time. Two cases of CLL were observed among males versus 1.2 expected. Only 1 bone cancer was observed compared with 0.2 cases expected. No sites were significantly below expectation.

Discussion

The overall risk of developing a second tumor after cancer of the eye was close to the expected figure. Cancers of the liver and gallbladder were the only sites which showed a significant excess but only among males. This observation might be due to a misclassification of metastatic liver lesions, but the excess risk remained throughout the observation period. An association between intraocular melanoma and CLL may exist because identical findings were seen for melanoma of the skin. The absence of an osteosarcoma risk is likely related to the small number of children with retinoblastoma in our study.

BRAIN AND NERVOUS SYSTEM (ICD-7, 193)

Tumors of the brain and nervous system account for 2.4% of all cancers in Denmark and are similar in both sexes (*2*). In 1978–80, the age-standardized incidence rate was 9.3 and 8.5/100,000 in males and females, respectively. All tumors of the cerebrospinal system are reported to the Registry and are included in the tabulations without regard to whether they are malignant or benign. Throughout the period of 1943–80, a slight increase in incidence was observed, which may, however, be an artifact due to improved detection over time. In 1963–72, the 5-year relative survival rates were 24–26% (*9*). Although tumor occurrence seems to be more common in urban than rural areas in Denmark, no substantial geographic variation has been observed (*1*).

Epidemiologic studies on tumors of the brain and nervous system have revealed few risk factors. Some rare heritable diseases predispose to these tumors. Radiation, rubber manufacturing, and other occupational chemical exposures have also been implicated (*15*), but few studies have considered the differences in tumor histology of these sites. Type-specific tumors of the nervous system should probably be regarded as distinct groups of diseases, each with individual incidence and survival rates, as well as specific risk factors. An earlier study (*16*) reported a relationship between meningioma and breast cancer that is possibly related to common hormonal factors.

Results

During the years 1943–80, the number of persons with tumors of the brain and nervous system who were eligible to be included in this analysis was 10,723. For males and females combined, the average age at diagnosis was 46 years. The average follow-up was 5.3 years, and the average year of diagnosis was 1965. Over 90% of the primary tumors were histologically confirmed. Although radiation therapy was given to 31% of the males and 25% of the females, surgery was the primary treatment for these tumors.

A total of 288 persons (or 2.8%) developed a second cancer (RR = 1.06; 95% CI = 0.94–1.19). Significant increases were seen for cancers of the kidney (RR = 3.2), bone (RR = 6.9), connective tissue (RR = 4.9), secondary brain tumors (RR = 2.0), and melanoma of the skin (RR = 2.5). The melanoma excess was seen only in females. Among males an increased risk was observed for leukemia, mainly due to an excess of CLL (RR = 3.2; 95% CI = 1.0–7.5). No clear trend in risk over time could be demonstrated for any of the sites mentioned. Among the 1,923 persons followed for 10 years or more, an elevated risk persisted for second tumors of the kidney (RR = 4.0), brain (1.5), bone (4.8), and connective tissue (7.7), and for CLL (1.5). An initial increased risk of cancer in the thyroid gland disappeared after 5 years of observation. The observed number of breast cancers was slightly below expectation (RR = 0.9).

Discussion

A nonsignificant 8% deficit of second tumors among men and a 14% excess among women was found following tumors of the brain and nervous system. Cancer of the kidney occurred in excess in both sexes. Brain tumors rarely metastasize to sites outside the central nervous system, whereas the brain is a frequent metastatic site for tumors originating elsewhere, especially from the lung, breast, and kidney. Because kidney cancer was excessive in all follow-up periods, it is unlikely that misdiagnosed primary cancer of the kidney is the only explanation for the association with brain tumors. However, the reason why kidney cancer was increased following tumors of the brain is not entirely clear.

A portion of the excess of bone and connective tissue cancer might be attributed to radiation therapy of the brain in 28% of the patients. The excess risk of melanoma was not expected and was seen only in women. Due to the fact that both brain tissue and melanocytes derive from the neural crest, it is possible that a common host susceptibility or underlying abnormality contributed to this finding. The reason for an excess of CLL among men is not known, although the numbers are small and chance might be involved when so many comparisons are made.

THYROID (ICD-7, 194)

Cancer of the thyroid is rare in Denmark and accounts for approximately 0.3% of all cancers in men and 0.6% in women. Between 1943 and 1980, the age-standardized incidence rates almost doubled. In 1978–80, the age-standardized rates were 0.9/100,000 man-years and 1.8/100,000 woman-years, i.e., women are twice as likely as men to develop this tumor (*1, 2*). The risk of thyroid cancer is low in Denmark compared with other Scandinavian countries and the United States (*17*).

Compared with other cancers, the prognosis after cancer of the thyroid is extremely favorable with an overall 5-year relative survival rate of about 75% (*5*). The prognosis depends on the age at diagnosis, with the elderly experiencing the poorest survival. To some extent, however, this difference in survival by age reflects the fact that anaplastic disease is more prevalent in the older age groups and has the worst prognosis of all thyroid cancers (*18*).

The only etiologic factor clearly related to thyroid cancer is ionizing radiation. Other etiologic hypotheses include sex hormones, prior thyroid disease, and genetic susceptibility (*18*). Although it would be valuable to consider each histomorphologic type separately, we were unable to do so because of the small numbers involved and because histopathologic classification has only been practiced during the later years of the observation period.

Results

Our present records include information on 1,935 persons who survived 2 or more months after a diagnosis of thyroid cancer in Denmark between 1943 and 1980. About 70% were women. The average age at diagnosis was 59 years, and the average follow-up was 5.6 years. Fifty percent of the patients initially received radiotherapy, including both external beam radiotherapy and radioiodine therapy.

A total of 78 (or 4.0%) of the thyroid cancer patients developed a second neoplasm. Of these, 87% were histologically verified. Both the first and the second primary cancers were histologically verified in 82% of the persons who developed multiple cancers. Based on the rates in the general population, 81 second cancers were expected (RR = 0.96; 95% CI = 0.76–1.20). The risk did not vary with time after diagnosis.

For both sexes combined, significantly increased RR were found for cancer of the brain and nervous system (3.0; 95% CI = 1.0–7.0) and NHL (4.4; 95% CI = 1.6–9.7). One-half ($n = 3$) of the patients with NHL were reported within the first year after initial diagnosis of thyroid cancer. A significant excess of colon cancer was observed in men (RR = 4.0; 95% CI = 1.7–7.9) but not in women (0.7). A deficit was noted for cancers of the lung (RR = 0.4; 95% CI = 0.1–1.2). The risks for cancer of the female breast (0.9) and for leukemia (1.5) were not significantly increased.

Discussion

The risk of developing a second primary cancer in persons with thyroid cancer was not greater than the risk of cancer expected on the basis of rates in the general population. Excess of NHL occurred in men and women. This association has not been reported previously, but because one-half the patients with NHL were diagnosed within the first year of observation, increased medical attention cannot be ruled out as an explanation.

Previous investigators (*19*) who studied women with cancer of the thyroid gland have reported a high risk of breast cancer, which suggests common etiologic factors. However, this hypothesis was not supported by our data which showed a slight deficit of breast cancer following thyroid cancer. They also observed an increased risk of kidney cancer subsequent to cancer of the thyroid gland. In our present investigation, we found a nonsignificant increased RR of 1.7 based on 4 kidney cancers. About 50% of the thyroid cancer patients received radiation therapy, so that radioactive iodine might theoretically be involved in the slightly increased risk of kidney cancer. Interestingly, no significant risk of leukemia was observed, although such an association with thyroid cancer has been reported in Denmark (*20*).

The significantly increased risk for colon cancer in men has not been seen previously. The risks of second cancers of the lung and the pancreas were below expectation and may be due to underreporting or our conservative coding practices in the Registry. Because the number of second cancers was small, chance might well be involved with several of the findings.

BONE (ICD-7, 196)

Between 1971 and 1980, an average of only 45 new cases of bone cancer were reported per year to the Registry. This represents 0.2% of all cancers and 21% of all sarcomas (*2*). Men are 1.3 times as likely to develop bone cancer as women. The age-standardized incidence rate changed little between 1943 and 1972; thereafter a decrease from 0.8 to 0.5/100,000 in women and from 1.1 to 0.7/100,000 in men in 1973–80 was seen. It is uncertain whether the decrease in incidence is real because the rate calculations were based on small numbers and the Registry coding practices were changed in 1978.

For men and women, the age-specific incidence shows a characteristic bimodal curve with a peak at age 15 to 19, a minimum around age 45, and a steady increase after the age of 50 years (*1*). This pattern represents different age-incidence characteristics for different histologic types of bone cancer. Osteogenic sarcoma is mainly a cancer of adolescence (10–20 yr of age), whereas chondrosarcomas and reticulum cell sarcomas appear after the age of 50 years (*21*). The few risk factors that have been identified for bone cancer include ionizing radiation, Paget's disease, genetic characteristics, and conditions related to the adolescent growth spurt (*21*).

Results

A total of 1,542 persons who developed bone cancer in Denmark between 1943 and 1980 were included in the study. The average follow-up was 5.6 years. Treatment involved surgery in about 60% and radiation in about 46% of the patients. Altogether, 44 persons developed second primary cancers, whereas 47.5 were expected on the basis of rates prevailing in the general population (RR = 0.93; 95% CI = 0.67–1.24).

Male patients with bone cancer developed 21 second cancers and 26.3 were expected. Among females, 23 new cancers were observed versus 21.2 expected. The overall RR risk did not vary with time after the initial diagnosis. There was a significant excess of second cancers of the kidney; 5 cases were observed versus 1.4 expected (RR = 3.5; 95% CI = 1.1–8.2). Four kidney cancers appeared 10 or more years after the first bone cancer. Eye cancer also occurred in excess, although the numbers were small (3 vs. 0.2). Although based on small numbers, cancers of the kidney and eye were elevated above expectation for both males and females. Among women, a significantly increased risk of lung cancer was detected based on 4 cases (RR = 4.5; 95% CI = 1.2–11).

Discussion

Patients with bone cancer were at no higher risk than the general population to develop a new cancer. However, a few individual sites were elevated above expectation. No significant deficits were noted. An excess of kidney cancer subsequent to bone cancer may be due to a slightly increased autopsy rate among cancer patients (*22*). Conceivably, radiotherapy might have contributed to this risk because 60% of the bone cancers occurred in the pelvis and lower limbs and the excess was concentrated among long-term survivors. The increased risk of eye cancer may suggest an influence of hereditary factors, especially if the eye cancers were retinoblastomas. To confirm this hypothesis, the histologic types of bone and eye cancers should be reviewed, as well as the ages at which they occurred. It is possible that the excess lung cancer risk, seen only in women, may have resulted from misclassification of metastases from the primary bone cancer. Investigators should focus future studies of bone cancer on specific histologies, sites of occurrence, age characteristics, and the determination of possible etiologic factors.

CONNECTIVE TISSUE (ICD-7, 197)

Malignant neoplasms of the connective tissue are rare and account for only 0.3% of all cancers in Denmark (*2*). During the period 1971–80, the Registry was notified of 68 new cases per year. The connective tissue comprises 31% of all reported sarcomas (bone cancer comprises 21%); one-half of the sarcomas are thus classified with carcinomas as occurring in the tissue of the specific organ site. The age-standardized incidence rates have declined slightly over time, and in 1978–80 the rate among males was 1.1/100,000 man-years and among females it was 0.7/100,000 woman-years. The decrease over time may in part be the result of an increase in the percentage of histologically verified tumors from 83% in 1943–47 to 99% in 1978–80 (*23*).

Connective tissue ranks sixth in cancer incidence among children under the age of 15, following cancer of the nervous system, leukemia, lymphoma, and cancer of the kidney and bone (*1*). For both males and females, the age-specific incidence increases with age, but a more pronounced increase is seen after the age of 40 years. No peak is seen in adolescence, contrary to that found for bone cancer. In Norway, the 5-year relative survival rate has increased slightly since 1953 and was 47% in males and 53% in females in 1968–75 (*5*). Little is known about the causes of connective tissue tumors, but ionizing radiation, genetic conditions, certain chemicals, such as phenoxyacetic acids seem involved to some extent (*24*).

Results

Our present data include the material on 2,318 persons who survived 2 or more months after diagnosis of connective tissue cancer in 1943–80. The average age at diagnosis was 52 years, and the average follow-up was 6.6 years for males and 8.5 years for females. In addition to surgery, radiation was frequently given as an initial treatment (41%). Overall, 123 second primary cancers were reported following involvement of the connective tissues and 122.5 were expected (RR = 1.00; 95% CI = 0.84–1.20). Male patients developed 60 second cancers compared with 61.3 expected on the basis of rates in the general population. Among females, 63 second cancers were observed compared with 61.2 expected. The risk of developing a second cancer increased significantly with time since the initial diagnosis ($P = .0003$ for trend) in both men and women. After 10 or more years of observation, the RR was 1.2 (95% CI = 0.9–1.6). Over 50% of the second cancers appeared 10 or more years after diagnosis of the first primary tumor. No site occurred significantly below expectation.

Increased risks were suggested for several sites. A total of 19 lung cancers were observed compared with 13.9 expected (RR = 1.4; 95% CI = 0.8–2.1). Lung cancer risk was elevated in men but not in women. Among females, 20 breast cancers were observed versus 13.3 expected (RR =

1.5; 95% CI = 0.9–2.3). One breast cancer also developed in a male after more than 10 years from the time of treatment for connective tissue cancer. The risk of female breast cancer increased with time and was significantly elevated among the 498 women surviving for more than 5 years (RR = 2.0; 95% CI = 1.2–3.1). An increased risk of NHL was based on only 6 observed lymphomas versus 2.0 expected (RR = 2.9; 95% CI = 1.1–6.4).

Discussion

The overall risk of a second cancer in patients with tumors of connective tissue was equal to that expected from the general population. Cancers of the lung and breast and NHL were elevated to some extent. The lung is the most common site for metastases of connective tissue tumors of the extremities, although retroperitoneal tumors may often spread first to the liver (*25*). Thus the small excess might be partly due to misdiagnosed metastatic lesions. An increased risk for breast cancer after connective tissue tumors was suggested, which is interesting in light of the excess of connective tissue cancer following cancer of the female breast (*26*). Possible explanations for this bidirectional association between cancers of the connective tissue and the breast include the effects of radiotherapy (*27*) or the presence of an unusual host susceptibility and tendency for these 2 cancers to cluster in families and individuals (*28*). Interestingly, radical mastectomy and the associated lymphedema in the extremities has been associated with increased risks of certain soft-tissue sarcomas, most notably lymphangiosarcomas (*29*). The significant excess risk of NHL among patients with tumors of connective tissue is based on few cases but is interesting in light of reports that chlorophenols and phenoxy herbicides might be risk factors for the development of soft tissue sarcomas (*30*) and malignant lymphomas (*31*).

SUMMARY

In this chapter, we attempted to evaluate a variety of diverse organs, such as malignant melanoma of the skin and cancers of the eye, brain, thyroid, bone, and connective tissue. The common characteristics of these cancers are their rarity and the many different histologies represented within each site. According to cell type of origin, the index sites fall naturally in 3 groups; a comparison of the pattern of second cancers in these groups would be enlightening. The eye, brain, and melanocytes develop from the neural tube. Slight excesses of CLL were observed subsequent to primary cancers of these neurally derived cancers. To our knowledge, this possible association has not been described previously. Second bone cancers also developed in excess following melanoma and cancers of the brain and eye, possibly due to misclassified metastases, unusual host susceptibility (*12*), or radiotherapy (*21*). Bone and connective tissue cancer account for approximately 50% of all sarcomas occurring in Denmark. Both sites showed decreased risks of second cancers of the digestive system which, when combined, were statistically significant (RR = 0.71; 95% CI = 0.51–0.96). Deficits were apparent for all digestive organs, except the stomach, but the implication of this finding is unclear.

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MELANOMA
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial malignant melanoma of the skin, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,857	4,354	7,211
No. who developed a second primary cancer	111	201	312
Average age at diagnosis of first cancer, yr	54	53	53
Average yr of diagnosis of first cancer	1969	1969	1969
Person-yr of follow-up	13,671	29,323	42,994
Average follow-up, yr	4.8	6.7	6.1
Percent given radiotherapy for first cancer	19	13	15

[a] ICD-7 code = 190.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial malignant melanoma of the skin in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	247	79.2
Only the first cancer	36	11.5
Only the second cancer	22	7.1
Neither first nor second cancer	7	2.2
Total second primary cancers	312	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

MELANOMA BOTH SEXES

TABLE 1C. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial malignant melanoma of the skin among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	7,211			5,927			2,800			1,459			7,211		
Person-yr in interval	6,594			16,114			10,066			10,219			42,994		
Second primary cancer site	O	E	O/F	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**34**	**43.98**	**0.8**	**130**	**109.41**	**1.2**	**75**	**72.41**	**1.0**	**73**	**84.06**	**0.9**	**312**	**309.85**	**1.0**
All excluding site of initial cancer	**34**	**43.29**	**0.8**	**128**	**107.63**	**1.2**	**74**	**71.20**	**1.0**	**72**	**82.68**	**0.9**	**308**	**304.80**	**1.0**
Buccal cavity, pharynx	**1**	**0.97**	**1.0**	**4**	**2.26**	**1.8**	**2**	**1.38**	**1.4**	**2**	**1.55**	**1.3**	**9**	**6.16**	**1.5**
Lip	0	0.40	0.0	2	0.87	2.3	0	0.50	0.0	0	0.52	0.0	2	2.29	0.9
Tongue	0	0.10	0.0	0	0.25	0.0	1	0.16	6.3	0	0.18	0.0	1	0.68	1.5
Salivary gland	0	0.12	0.0	1	0.29	3.4	0	0.18	0.0	1	0.19	5.3	2	0.79	2.5
Gum, other mouth	0	0.18	0.0	1	0.45	2.2	1	0.30	3.3	0	0.38	0.0	2	1.30	1.5
Pharynx	1	0.17	5.9	0	0.40	0.0	0	0.25	0.0	1	0.29	3.4	2	1.10	1.8
Digestive system	**7**	**14.37**	**0.5**	**49**	**34.81**	**1.4**^{b}	**21**	**22.53**	**0.9**	**19**	**26.59**	**0.7**	**96**	**98.30**	**1.0**
Esophagus	0	0.51	0.0	0	1.19	0.0	0	0.73	0.0	0	0.83	0.0	0	3.27	0.0
Stomach	5	3.84	1.3	9	8.84	1.0	4	5.33	0.8	2	5.77	0.3	20	23.77	0.8
Colon	0	4.04	0.0^{b}	15	10.14	1.5	9	6.88	1.3	6	8.50	0.7	30	29.54	1.0
Rectum	1	2.89	0.3	14	6.96	2.0^{b}	4	4.43	0.9	8	5.14	1.6	27	19.42	1.4
Liver, biliary	1	1.04	1.0	2	2.65	0.8	0	1.84	0.0	1	2.30	0.4	4	7.82	0.5
Pancreas	0	1.52	0.0	3	3.79	0.8	1	2.55	0.4	2	3.16	0.6	6	11.02	0.5
Respiratory system	**2**	**5.39**	**0.4**	**11**	**12.89**	**0.9**	**8**	**8.02**	**1.0**	**12**	**9.30**	**1.3**	**33**	**35.60**	**0.9**
Nasal cavities, sinuses	0	0.10	0.0	0	0.22	0.0	0	0.14	0.0	0	0.15	0.0	0	0.61	0.0
Larynx	0	0.36	0.0	0	0.84	0.0	0	0.50	0.0	0	0.56	0.0	0	2.25	0.0
Trachea, bronchus, lung	2	4.67	0.4	10	11.21	0.9	7	6.98	1.0	12	8.14	1.5	31	31.01	1.0
Female breast	7	5.58	1.3	15	15.26	1.0	13	11.20	1.2	13	13.00	1.0	48	45.04	1.1
Female genital tract	**6**	**5.30**	**1.1**	**18**	**14.34**	**1.3**	**11**	**10.29**	**1.1**	**7**	**11.42**	**0.6**	**42**	**41.35**	**1.0**
Cervix uteri	4	2.04	2.0	4	5.47	0.7	4	3.76	1.1	0	3.70	0.0^{b}	12	14.97	0.8
Corpus uteri	1	1.39	0.7	9	3.82	2.4^{b}	4	2.85	1.4	3	3.42	0.9	17	11.48	1.5
Uterus, NOS	0	0.09	0.0	1	0.23	4.4	0	0.15	0.0	0	0.17	0.0	1	0.64	1.6
Ovary, fallopian tubes	1	1.49	0.7	4	4.07	1.0	2	2.98	0.7	4	3.44	1.2	11	11.99	0.9
Prostate gland	1	2.42	0.4	4	5.40	0.7	3	3.11	1.0	3	3.65	0.8	11	14.58	0.8
Testis	0	0.18	0.0	0	0.39	0.0	0	0.19	0.0	0	0.19	0.0	0	0.95	0.0
Kidney, renal pelvis, ureter	1	1.27	0.8	4	3.16	1.3	5	2.09	2.4	2	2.49	0.8	12	9.02	1.3
Bladder, other urinary	5	2.26	2.2	5	5.44	0.9	3	3.43	0.9	2	4.07	0.5	15	15.20	1.0
Melanoma of the skin	0	0.69	0.0	2	1.78	1.1	1	1.21	0.8	1	1.38	0.7	4	5.05	0.8
Eye	1	0.13	7.7	1	0.31	3.2	0	0.20	0.0	0	0.23	0.0	2	0.88	2.3
Brain, central nervous system	0	0.96	0.0	3	2.40	1.3	2	1.59	1.3	3	1.77	1.7	8	6.71	1.2
Thyroid gland	0	0.23	0.0	1	0.58	1.7	0	0.40	0.0	1	0.47	2.1	2	1.67	1.2
Bone	1	0.08	12.5	1	0.19	5.3	0	0.11	0.0	0	0.12	0.0	2	0.51	3.9
Connective tissue	0	0.15	0.0	1	0.38	2.6	0	0.23	0.0	0	0.26	0.0	1	1.02	1.0
Lymphatic, hematopoietic system	**1**	**2.58**	**0.4**	**6**	**6.34**	**0.9**	**3**	**4.15**	**0.7**	**5**	**4.92**	**1.0**	**15**	**17.98**	**0.8**
Non-Hodgkin's lymphoma	0	0.74	0.0	1	1.84	0.5	2	1.21	1.7	2	1.46	1.4	5	5.25	1.0
Hodgkin's disease	0	0.23	0.0	1	0.55	1.8	0	0.35	0.0	0	0.37	0.0	1	1.50	0.7
Multiple myeloma	0	0.47	0.0	1	1.16	0.9	0	0.78	0.0	0	0.94	0.0	1	3.34	0.3
Leukemias	1	1.11	0.9	3	2.71	1.1	1	1.78	0.6	3	2.10	1.4	8	7.71	1.0
Chronic lymphocytic	1	0.52	1.9	3	1.25	2.4	1	0.81	1.2	2	0.96	2.1	7	3.53	2.0
Acute nonlymphocytic	0	0.33	0.0	0	0.84	0.0	0	0.57	0.0	1	0.70	1.4	1	2.44	0.4

[a] ICD-7 code = 190.
[b] $P < .05$.

MELANOMA
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial malignant melanoma of the skin among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,857			2,227			849			396			2,857		
Person-yr in interval	2,552			5,471			2,854			2,794			13,671		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**15**	**19.27**	**0.8**	**50**	**42.66**	**1.2**	**23**	**23.81**	**1.0**	**23**	**26.16**	**0.9**	**111**	**111.90**	**1.0**
All excluding site of initial cancer	**15**	**19.04**	**0.8**	**48**	**42.15**	**1.1**	**22**	**23.53**	**0.9**	**22**	**25.86**	**0.9**	**107**	**110.59**	**1.0**
Buccal cavity, pharynx	**0**	**0.65**	**0.0**	**2**	**1.42**	**1.4**	**1**	**0.77**	**1.3**	**0**	**0.80**	**0.0**	3	**3.64**	**0.8**
Lip	0	0.35	0.0	1	0.75	1.3	0	0.41	0.0	0	0.41	0.0	1	1.92	0.5
Tongue	0	0.05	0.0	0	0.11	0.0	1	0.06	17.1	0	0.06	0.0	1	0.27	3.6
Salivary gland	0	0.05	0.0	0	0.11	0.0	0	0.06	0.0	0	0.06	0.0	0	0.29	0.0
Gum, other mouth	0	0.09	0.0	1	0.21	4.9	0	0.12	0.0	0	0.13	0.0	1	0.54	1.9
Pharynx	0	0.11	0.0	0	0.24	0.0	0	0.13	0.0	0	0.14	0.0	0	0.62	0.0
Digestive system	**4**	**6.93**	**0.6**	**22**	**15.07**	**1.5**	**9**	**8.27**	**1.1**	**7**	**8.95**	**0.8**	**42**	**39.22**	**1.1**
Esophagus	0	0.31	0.0	0	0.67	0.0	0	0.36	0.0	0	0.37	0.0	0	1.71	0.0
Stomach	3	2.10	1.4	2	4.44	0.5	1	2.35	0.4	0	2.40	0.0	6	11.29	0.5
Colon	0	1.62	0.0	7	3.60	1.9	6	2.03	3.0^b	3	2.30	1.3	16	9.55	1.7
Rectum	1	1.55	0.6	8	3.37	2.4^b	2	1.85	1.1	4	1.99	2.0	15	8.75	1.7
Liver, biliary	0	0.39	0.0	0	0.87	0.0	0	0.50	0.0	0	0.57	0.0	0	2.33	0.0
Pancreas	0	0.73	0.0	2	1.64	1.2	0	0.93	0.0	0	1.05	0.0	2	4.35	0.5
Respiratory system	**1**	**4.05**	**0.2**	**9**	**9.14**	**1.0**	**3**	**5.16**	**0.6**	**7**	**5.65**	**1.2**	**20**	**24.00**	**0.8**
Nasal cavities, sinuses	0	0.06	0.0	0	0.12	0.0	0	0.07	0.0	0	0.07	0.0	0	0.32	0.0
Larynx	0	0.30	0.0	0	0.67	0.0	0	0.37	0.0	0	0.40	0.0	0	1.74	0.0
Trachea, bronchus, lung	1	3.52	0.3	8	7.98	1.0	2	4.51	0.4	7	4.95	1.4	18	20.96	0.9
Prostate gland	1	2.42	0.4	4	5.40	0.7	3	3.11	1.0	3	3.65	0.8	11	14.58	0.8
Testis	0	0.18	0.0	0	0.39	0.0	0	0.19	0.0	0	0.19	0.0	0	0.95	0.0
Kidney, renal pelvis, ureter	1	0.65	1.5	1	1.45	0.7	3	0.82	3.6	1	0.91	1.1	6	3.83	1.6
Bladder, other urinary	5	1.61	3.1^b	4	3.64	1.1	1	2.08	0.5	1	2.34	0.4	11	9.67	1.1
Melanoma of the skin	0	0.23	0.0	2	0.51	3.9	1	0.28	3.6	1	0.30	3.4	4	1.31	3.1
Eye	0	0.06	0.0	0	0.13	0.0	0	0.07	0.0	0	0.08	0.0	0	0.35	0.0
Brain, central nervous system	0	0.40	0.0	1	0.88	1.1	1	0.48	2.1	0	0.49	0.0	2	2.24	0.9
Thyroid gland	0	0.06	0.0	0	0.13	0.0	0	0.07	0.0	0	0.08	0.0	0	0.33	0.0
Bone	1	0.04	26.0	1	0.08	12.2	0	0.04	0.0	0	0.04	0.0	2	0.21	9.6^b
Connective tissue	0	0.07	0.0	0	0.16	0.0	0	0.08	0.0	0	0.09	0.0	0	0.40	0.0
Lymphatic, hematopoietic system	**1**	**1.30**	**0.8**	**4**	**2.87**	**1.4**	**1**	**1.61**	**0.6**	**1**	**1.77**	**0.6**	**7**	**7.54**	**0.9**
Non-Hodgkin's lymphoma	0	0.35	0.0	1	0.78	1.3	0	0.43	0.0	0	0.47	0.0	1	2.03	0.5
Hodgkin's disease	0	0.12	0.0	0	0.25	0.0	0	0.14	0.0	0	0.14	0.0	0	0.65	0.0
Multiple myeloma	0	0.23	0.0	1	0.50	2.0	0	0.29	0.0	0	0.32	0.0	1	1.34	0.7
Leukemias	1	0.59	1.7	2	1.30	1.5	1	0.74	1.4	1	0.82	1.2	5	3.45	1.4
Chronic lymphocytic	1	0.31	3.2	2	0.68	2.9	1	0.39	2.6	1	0.43	2.3	5	1.81	2.8
Acute nonlymphocytic	0	0.15	0.0	0	0.35	0.0	0	0.20	0.0	0	0.23	0.0	0	0.94	0.0

[a] ICD-7 code = 190.
[b] $P < .05$.

MELANOMA
FEMALES

TABLE 1E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial malignant melanoma of the skin among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	4,354			3,700			1,951			1,063			4,354		
Person-yr in interval	4,042			10,643			7,212			7,426			29,323		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**19**	**24.71**	**0.8**	**80**	**66.75**	**1.2**	**52**	**48.60**	**1.1**	**50**	**57.90**	**0.9**	**201**	**197.95**	**1.0**
All excluding site of initial cancer	**19**	**24.25**	**0.8**	**80**	**65.48**	**1.2**	**52**	**47.67**	**1.1**	**50**	**56.82**	**0.9**	**201**	**194.21**	**1.0**
Buccal cavity, pharynx	**1**	**0.32**	**3.1**	**2**	**0.84**	**2.4**	**1**	**0.61**	**1.6**	**2**	**0.75**	**2.7**	**6**	**2.52**	**2.4**
Lip	0	0.05	0.0	1	0.12	8.2	0	0.09	0.0	0	0.11	0.0	1	0.37	2.7
Tongue	0	0.05	0.0	0	0.14	0.0	0	0.10	0.0	0	0.12	0.0	0	0.41	0.0
Salivary gland	0	0.07	0.0	1	0.18	5.4	0	0.12	0.0	1	0.13	7.9	2	0.50	4.0
Gum, other mouth	0	0.09	0.0	0	0.24	0.0	1	0.18	5.5	0	0.25	0.0	1	0.76	1.3
Pharynx	1	0.06	16.5	0	0.16	0.0	0	0.12	0.0	1	0.15	6.9	2	0.48	4.1
Digestive system	**3**	**7.44**	**0.4**	**27**	**19.74**	**1.4**	**12**	**14.26**	**0.8**	**12**	**17.64**	**0.7**	**54**	**59.08**	**0.9**
Esophagus	0	0.20	0.0	0	0.52	0.0	0	0.37	0.0	0	0.46	0.0	0	1.56	0.0
Stomach	2	1.74	1.2	7	4.40	1.6	3	2.98	1.0	2	3.37	0.6	14	12.48	1.1
Colon	0	2.42	0.0	8	6.54	1.2	3	4.85	0.6	3	6.20	0.5	14	19.99	0.7
Rectum	0	1.34	0.0	6	3.59	1.7	2	2.58	0.8	4	3.15	1.3	12	10.67	1.1
Liver, biliary	1	0.65	1.5	2	1.78	1.1	0	1.34	0.0	1	1.73	0.6	4	5.49	0.7
Pancreas	0	0.79	0.0	1	2.15	0.5	1	1.62	0.6	2	2.11	0.9	4	6.67	0.6
Respiratory system	**1**	**1.34**	**0.7**	**2**	**3.75**	**0.5**	**5**	**2.86**	**1.7**	**5**	**3.65**	**1.4**	**13**	**11.60**	**1.1**
Nasal cavities, sinuses	0	0.04	0.0	0	0.10	0.0	0	0.07	0.0	0	0.08	0.0	0	0.29	0.0
Larynx	0	0.06	0.0	0	0.17	0.0	0	0.13	0.0	0	0.16	0.0	0	0.51	0.0
Trachea, bronchus, lung	1	1.15	0.9	2	3.23	0.6	5	2.47	2.0	5	3.19	1.6	13	10.05	1.3
Female breast	7	5.58	1.3	15	15.26	1.0	13	11.20	1.2	13	13.00	1.0	48	45.04	1.1
Female genital tract	**6**	**5.30**	**1.1**	**18**	**14.34**	**1.3**	**11**	**10.29**	**1.1**	**7**	**11.42**	**0.6**	**42**	**41.35**	**1.0**
Cervix uteri	4	2.04	2.0	4	5.47	0.7	4	3.76	1.1	0	3.70	0.0[b]	12	14.97	0.8
Corpus uteri	1	1.39	0.7	9	3.82	2.4[b]	4	2.85	1.4	3	3.42	0.9	17	11.48	1.5
Uterus, NOS	0	0.09	0.0	1	0.23	4.4	0	0.15	0.0	0	0.17	0.0	1	0.64	1.6
Ovary, fallopian tubes	1	1.49	0.7	4	4.07	1.0	2	2.98	0.7	4	3.44	1.2	11	11.99	0.9
Kidney, renal pelvis, ureter	0	0.62	0.0	3	1.71	1.8	2	1.27	1.6	1	1.58	0.6	6	5.19	1.2
Bladder, other urinary	0	0.65	0.0	1	1.80	0.6	2	1.35	1.5	1	1.73	0.6	4	5.53	0.7
Melanoma of the skin	0	0.46	0.0	0	1.27	0.0	0	0.93	0.0	0	1.08	0.0	0	3.74	0.0[b]
Eye	1	0.07	14.7	1	0.18	5.5	0	0.13	0.0	0	0.15	0.0	2	0.53	3.8
Brain, central nervous system	0	0.56	0.0	2	1.52	1.3	1	1.11	0.9	3	1.28	2.3	6	4.47	1.3
Thyroid gland	0	0.17	0.0	1	0.45	2.2	0	0.33	0.0	1	0.39	2.6	2	1.34	1.5
Bone	0	0.04	0.0	0	0.11	0.0	0	0.07	0.0	0	0.08	0.0	0	0.30	0.0
Connective tissue	0	0.08	0.0	1	0.22	4.6	0	0.15	0.0	0	0.17	0.0	1	0.62	1.6
Lymphatic, hematopoietic system	**0**	**1.28**	**0.0**	**2**	**3.47**	**0.6**	**2**	**2.54**	**0.8**	**4**	**3.15**	**1.3**	**8**	**10.44**	**0.8**
Non-Hodgkin's lymphoma	0	0.39	0.0	0	1.06	0.0	2	0.78	2.5	2	0.99	2.0	4	3.22	1.2
Hodgkin's disease	0	0.11	0.0	1	0.30	3.3	0	0.21	0.0	0	0.23	0.0	1	0.85	1.2
Multiple myeloma	0	0.24	0.0	0	0.66	0.0	0	0.49	0.0	0	0.62	0.0	0	2.00	0.0
Leukemias	0	0.52	0.0	1	1.41	0.7	0	1.04	0.0	2	1.28	1.6	3	4.26	0.7
Chronic lymphocytic	0	0.21	0.0	1	0.57	1.8	0	0.42	0.0	1	0.53	1.9	2	1.72	1.2
Acute nonlymphocytic	0	0.18	0.0	0	0.49	0.0	0	0.37	0.0	1	0.47	2.1	1	1.50	0.7

[a] ICD-7 code = 190.

[b] $P < .05$.

EYE
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the eye, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	966	818	1,784
No. who developed a second primary cancer	72	47	119
Average age at diagnosis of first cancer, yr	54	54	54
Average yr of diagnosis of first cancer	1963	1963	1963
Person-yr of follow-up	7,696	6,897	14,593
Average follow-up, yr	8.0	8.4	8.2
Percent given radiotherapy for first cancer	16	13	14

[a] ICD-7 code = 192.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the eye in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	84	70.6
Only the first cancer	28	23.5
Only the second cancer	2	1.7
Neither first nor second cancer	5	4.2
Total second primary cancers	119	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

EYE
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the eye among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,784			1,561			889			549			1,784		
Person-yr in interval	1,669			4,691			3,456			4,777			14,593		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**11**	**13.05**	**0.8**	**35**	**36.96**	**0.9**	**25**	**27.96**	**0.9**	**48**	**40.45**	**1.2**	**119**	**118.42**	**1.0**
All excluding site of initial cancer	**11**	**13.00**	**0.8**	**35**	**36.84**	**1.0**	**25**	**27.88**	**0.9**	**48**	**40.34**	**1.2**	**119**	**118.06**	**1.0**
Buccal cavity, pharynx	**0**	**0.33**	**0.0**	**0**	**0.91**	**0.0**	**1**	**0.66**	**1.5**	**2**	**0.93**	**2.2**	**3**	**2.84**	**1.1**
Lip	0	0.15	0.0	0	0.42	0.0	1	0.30	3.3	2	0.41	4.9	3	1.29	2.3
Tongue	0	0.03	0.0	0	0.09	0.0	0	0.07	0.0	0	0.09	0.0	0	0.27	0.0
Salivary gland	0	0.04	0.0	0	0.11	0.0	0	0.08	0.0	0	0.10	0.0	0	0.33	0.0
Gum, other mouth	0	0.05	0.0	0	0.15	0.0	0	0.11	0.0	0	0.18	0.0	0	0.49	0.0
Pharynx	0	0.05	0.0	0	0.15	0.0	0	0.11	0.0	0	0.15	0.0	0	0.45	0.0
Digestive system	**5**	**4.77**	**1.0**	**14**	**13.41**	**1.0**	**9**	**10.02**	**0.9**	**27**	**14.23**	**1.9**[b]	**55**	**42.42**	**1.3**
Esophagus	1	0.18	5.6	1	0.51	2.0	0	0.37	0.0	0	0.51	0.0	2	1.57	1.3
Stomach	1	1.45	0.7	3	4.00	0.8	2	2.85	0.7	6	3.65	1.6	12	11.95	1.0
Colon	1	1.20	0.8	1	3.43	0.3	3	2.67	1.1	7	4.05	1.7	12	11.36	1.1
Rectum	1	0.98	1.0	5	2.77	1.8	1	2.06	0.5	5	2.85	1.8	12	8.66	1.4
Liver, biliary	1	0.30	3.3	3	0.87	3.4	2	0.70	2.9	3	1.09	2.8	9	2.97	3.0[b]
Pancreas	0	0.46	0.0	1	1.35	0.7	1	1.05	1.0	4	1.63	2.5	6	4.50	1.3
Respiratory system	**3**	**1.78**	**1.7**	**5**	**5.06**	**1.0**	**2**	**3.87**	**0.5**	**5**	**6.04**	**0.8**	**15**	**16.74**	**0.9**
Nasal cavities, sinuses	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.08	0.0	0	0.26	0.0
Larynx	1	0.12	8.3	1	0.33	3.0	0	0.24	0.0	0	0.37	0.0	2	1.06	1.9
Trachea, bronchus, lung	2	1.54	1.3	4	4.38	0.9	2	3.36	0.6	5	5.28	0.9	13	14.57	0.9
Female breast	2	1.12	1.8	4	3.20	1.3	2	2.40	0.8	2	3.35	0.6	10	10.07	1.0
Female genital tract	**1**	**1.07**	**0.9**	**4**	**3.04**	**1.3**	**4**	**2.22**	**1.8**	**1**	**2.82**	**0.4**	**10**	**9.13**	**1.1**
Cervix uteri	1	0.37	2.7	3	1.04	2.9	0	0.73	0.0	0	0.84	0.0	4	2.98	1.3
Corpus uteri	0	0.30	0.0	0	0.85	0.0	3	0.64	4.7	0	0.81	0.0	3	2.59	1.2
Uterus, NOS	0	0.02	0.0	0	0.07	0.0	0	0.04	0.0	0	0.06	0.0	0	0.20	0.0
Ovary, fallopian tubes	0	0.31	0.0	0	0.89	0.0	1	0.67	1.5	1	0.89	1.1	2	2.76	0.7
Prostate gland	0	1.01	0.0	3	2.91	1.0	3	2.35	1.3	1	3.44	0.3	7	9.72	0.7
Testis	0	0.04	0.0	0	0.10	0.0	0	0.07	0.0	0	0.14	0.0	0	0.35	0.0
Kidney, renal pelvis, ureter	0	0.39	0.0	0	1.11	0.0	0	0.85	0.0	1	1.25	0.8	1	3.59	0.3
Bladder, other urinary	0	0.75	0.0	1	2.14	0.5	1	1.67	0.6	2	2.60	0.8	4	7.16	0.6
Melanoma of the skin	0	0.14	0.0	1	0.38	2.6	1	0.30	3.3	1	0.46	2.2	3	1.28	2.3
Eye	0	0.05	0.0	0	0.12	0.0	0	0.08	0.0	0	0.11	0.0	0	0.36	0.0
Brain, central nervous system	0	0.25	0.0	0	0.69	0.0	0	0.51	0.0	0	0.71	0.0	0	2.16	0.0
Thyroid gland	0	0.06	0.0	0	0.16	0.0	0	0.13	0.0	0	0.19	0.0	0	0.54	0.0
Bone	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	1	0.08	12.5	1	0.23	4.3
Connective tissue	0	0.05	0.0	0	0.13	0.0	0	0.10	0.0	0	0.13	0.0	0	0.40	0.0
Lymphatic, hematopoietic system	**0**	**0.79**	**0.0**	**0**	**2.24**	**0.0**	**2**	**1.73**	**1.2**	**3**	**2.59**	**1.2**	**5**	**7.35**	**0.7**
Non-Hodgkin's lymphoma	0	0.21	0.0	0	0.60	0.0	0	0.46	0.0	0	0.71	0.0	0	1.98	0.0
Hodgkin's disease	0	0.06	0.0	0	0.17	0.0	0	0.13	0.0	1	0.19	5.3	1	0.56	1.8
Multiple myeloma	0	0.14	0.0	0	0.42	0.0	0	0.34	0.0	0	0.49	0.0	0	1.39	0.0
Leukemias	0	0.36	0.0	0	1.03	0.0	2	0.80	2.5	2	1.16	1.7	4	3.35	1.2
Chronic lymphocytic	0	0.18	0.0	0	0.51	0.0	2	0.40	5.0	0	0.59	0.0	2	1.69	1.2
Acute nonlymphocytic	0	0.09	0.0	0	0.26	0.0	0	0.21	0.0	0	0.33	0.0	0	0.88	0.0

[a] ICD-7 code = 192.

[b] $P < .05$.

BRAIN
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the brain or central nervous system (including benign tumors), 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	5,260	5,013	10,273
No. who developed a second primary cancer	95	193	288
Average age at diagnosis of first cancer, yr	45	47	46
Average yr of diagnosis of first cancer	1965	1965	1965
Person-yr of follow-up	22,365	30,246	52,611
Average follow-up, yr	4.3	6.0	5.3
Percent given radiotherapy for first cancer	31	25	28

[a] ICD-7 code = 193.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the brain or central nervous system (including benign tumors) in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	241	83.4
Only the first cancer	22	7.6
Only the second cancer	22	7.6
Neither first nor second cancer	4	1.4
Total second primary cancers	289	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

BRAIN
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the brain or central nervous system (including benign tumors) among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	10,273			5,560			3,005			1,923			10,273		
Person-yr in interval	7,503			15,624			12,001			17,482			52,611		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**27**	**31.75**	**0.9**	**62**	**63.77**	**1.0**	**67**	**59.10**	**1.1**	**132**	**116.96**	**1.1**	**288**	**271.58**	**1.1**
All excluding site of initial cancer	**23**	**30.80**	**0.7**	**60**	**61.89**	**1.0**	**63**	**57.52**	**1.1**	**128**	**114.25**	**1.1**	**274**	**264.47**	**1.0**
Buccal cavity, pharynx	**1**	**0.78**	**1.3**	**1**	**1.44**	**0.7**	**2**	**1.25**	**1.6**	**0**	**2.33**	**0.0**	**4**	**5.79**	**0.7**
Lip	0	0.34	0.0	1	0.59	1.7	2	0.50	4.0	0	0.86	0.0	3	2.29	1.3
Tongue	0	0.07	0.0	0	0.14	0.0	0	0.13	0.0	0	0.26	0.0	0	0.59	0.0
Salivary gland	1	0.11	9.1	0	0.22	0.0	0	0.19	0.0	0	0.31	0.0	1	0.84	1.2
Gum, other mouth	0	0.12	0.0	0	0.23	0.0	0	0.22	0.0	0	0.49	0.0	0	1.06	0.0
Pharynx	0	0.14	0.0	0	0.26	0.0	0	0.22	0.0	0	0.41	0.0	0	1.03	0.0
Digestive system	**3**	**9.31**	**0.3**[b]	**8**	**18.10**	**0.4**[b]	**25**	**17.44**	**1.4**	**31**	**36.51**	**0.8**	**67**	**81.35**	**0.8**
Esophagus	0	0.33	0.0	0	0.59	0.0	1	0.56	1.8	2	1.16	1.7	3	2.64	1.1
Stomach	0	2.42	0.0	2	4.48	0.4	5	4.20	1.2	7	8.04	0.9	14	19.14	0.7
Colon	1	2.52	0.4	3	5.12	0.6	7	5.06	1.4	8	11.30	0.7	19	23.98	0.8
Rectum	1	2.00	0.5	2	3.85	0.5	6	3.63	1.7	4	7.23	0.6	13	16.70	0.8
Liver, biliary	0	0.65	0.0	0	1.33	0.0	3	1.36	2.2	6	3.16	1.9	9	6.50	1.4
Pancreas	1	1.02	1.0	0	2.02	0.0	2	1.99	1.0	3	4.40	0.7	6	9.43	0.6
Respiratory system	**4**	**4.43**	**0.9**	**5**	**8.00**	**0.6**	**4**	**7.34**	**0.5**	**13**	**14.52**	**0.9**	**26**	**34.30**	**0.8**
Nasal cavities, sinuses	0	0.08	0.0	1	0.14	7.1	0	0.13	0.0	0	0.23	0.0	1	0.58	1.7
Larynx	0	0.31	0.0	1	0.55	1.8	0	0.48	0.0	0	0.90	0.0	1	2.24	0.4
Trachea, bronchus, lung	4	3.87	1.0	3	6.96	0.4	4	6.40	0.6	13	12.73	1.0	24	29.95	0.8
Female breast	1	3.99	0.3	11	9.18	1.2	4	8.47	0.5	17	16.54	1.0	33	38.17	0.9
Female genital tract	**4**	**4.28**	**0.9**	**9**	**9.82**	**0.9**	**9**	**8.78**	**1.0**	**18**	**15.33**	**1.2**	**40**	**38.21**	**1.0**
Cervix uteri	1	1.76	0.6	3	4.06	0.7	3	3.38	0.9	4	5.18	0.8	11	14.39	0.8
Corpus uteri	2	1.12	1.8	4	2.56	1.6	3	2.40	1.2	6	4.43	1.4	15	10.51	1.4
Uterus, NOS	0	0.06	0.0	0	0.13	0.0	0	0.12	0.0	0	0.22	0.0	0	0.53	0.0
Ovary, fallopian tubes	1	1.16	0.9	2	2.66	0.8	2	2.47	0.8	7	4.60	1.5	12	10.88	1.1
Prostate gland	0	1.31	0.0	1	2.26	0.4	0	2.23	0.0	6	4.74	1.3	7	10.54	0.7
Testis	0	0.22	0.0	1	0.44	2.3	1	0.31	3.2	1	0.53	1.9	3	1.50	2.0
Kidney, renal pelvis, ureter	4	0.94	4.3[b]	2	1.83	1.1	6	1.73	3.5[b]	14	3.54	4.0[b]	26	8.05	3.2[b]
Bladder, other urinary	3	1.63	1.8	3	3.01	1.0	3	2.85	1.1	6	5.98	1.0	15	13.47	1.1
Melanoma of the skin	0	0.51	0.0	3	1.08	2.8	2	0.94	2.1	6	1.88	3.2[b]	11	4.40	2.5[b]
Eye	0	0.11	0.0	0	0.22	0.0	0	0.19	0.0	0	0.35	0.0	0	0.88	0.0
Brain, central nervous system	4	0.95	4.2[b]	2	1.88	1.1	4	1.58	2.5	4	2.71	1.5	14	7.11	2.0[b]
Thyroid gland	1	0.16	6.3	3	0.34	8.8[b]	0	0.32	0.0	0	0.66	0.0	4	1.50	2.7
Bone	0	0.07	0.0	2	0.16	12.5[b]	1	0.13	7.7	1	0.21	4.8	4	0.58	6.9[b]
Connective tissue	0	0.14	0.0	2	0.27	7.4	0	0.22	0.0	3	0.39	7.7[b]	5	1.03	4.9[b]
Lymphatic, hematopoietic system	**2**	**1.98**	**1.0**	**8**	**3.90**	**2.1**	**5**	**3.59**	**1.4**	**5**	**7.17**	**0.7**	**20**	**16.65**	**1.2**
Non-Hodgkin's lymphoma	0	0.55	0.0	4	1.10	3.6	0	1.02	0.0	1	2.11	0.5	5	4.78	1.0
Hodgkin's disease	0	0.23	0.0	0	0.47	0.0	2	0.40	5.0	0	0.65	0.0	2	1.74	1.1
Multiple myeloma	2	0.33	6.1	0	0.65	0.0	0	0.64	0.0	0	1.34	0.0	2	2.96	0.7
Leukemias	0	0.84	0.0	4	1.64	2.4	3	1.50	2.0	4	3.01	1.3	11	7.00	1.6
Chronic lymphocytic	0	0.35	0.0	2	0.65	3.1	3	0.63	4.8	2	1.33	1.5	7	2.96	2.4
Acute nonlymphocytic	0	0.25	0.0	1	0.52	1.9	0	0.47	0.0	2	0.99	2.0	3	2.23	1.3

[a] ICD-7 code = 193.
[b] $P < .05$.

BRAIN
MALES

Table 3D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the brain or central nervous system (including benign tumors) among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,260			2,617			1,285			770			5,260		
Person-yr in interval	3,720			6,948			4,962			6,735			22,365		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**13**	**14.76**	**0.9**	**22**	**24.95**	**0.9**	**23**	**22.04**	**1.0**	**37**	**41.17**	**0.9**	**95**	**102.92**	**0.9**
All excluding site of initial cancer	**10**	**14.28**	**0.7**	**21**	**24.13**	**0.9**	**22**	**21.41**	**1.0**	**35**	**40.16**	**0.9**	**88**	**99.98**	**0.9**
Buccal cavity, pharynx	**0**	**0.57**	**0.0**	**1**	**0.96**	**1.0**	**2**	**0.79**	**2.5**	**0**	**1.35**	**0.0**	**3**	**3.67**	**0.8**
Lip	0	0.31	0.0	1	0.52	1.9	2	0.43	4.6	0	0.71	0.0	3	1.98	1.5
Tongue	0	0.04	0.0	0	0.07	0.0	0	0.06	0.0	0	0.10	0.0	0	0.26	0.0
Salivary gland	0	0.05	0.0	0	0.09	0.0	0	0.07	0.0	0	0.11	0.0	0	0.33	0.0
Gum, other mouth	0	0.07	0.0	0	0.12	0.0	0	0.10	0.0	0	0.19	0.0	0	0.48	0.0
Pharynx	0	0.10	0.0	0	0.16	0.0	0	0.13	0.0	0	0.23	0.0	0	0.62	0.0
Digestive system	**1**	**4.86**	**0.2**	**4**	**8.10**	**0.5**	**9**	**7.18**	**1.3**	**11**	**13.11**	**0.8**	**25**	**33.24**	**0.8**
Esophagus	0	0.22	0.0	0	0.36	0.0	0	0.32	0.0	1	0.56	1.8	1	1.46	0.7
Stomach	0	1.44	0.0	2	2.37	0.8	3	2.04	1.5	1	3.41	0.3	6	9.26	0.6
Colon	0	1.08	0.0	2	1.82	1.1	2	1.66	1.2	4	3.24	1.2	8	7.79	1.0
Rectum	1	1.12	0.9	0	1.87	0.0	2	1.65	1.2	1	2.99	0.3	4	7.62	0.5
Liver, biliary	0	0.27	0.0	0	0.46	0.0	2	0.43	4.6	2	0.86	2.3	4	2.03	2.0
Pancreas	0	0.55	0.0	0	0.93	0.0	0	0.85	0.0	1	1.64	0.6	1	3.97	0.3
Respiratory system	**3**	**3.56**	**0.8**	**4**	**5.96**	**0.7**	**3**	**5.33**	**0.6**	**5**	**10.03**	**0.5**	**15**	**24.88**	**0.6**[b]
Nasal cavities, sinuses	0	0.05	0.0	1	0.08	12.2	0	0.07	0.0	0	0.12	0.0	1	0.32	3.1
Larynx	0	0.27	0.0	0	0.45	0.0	0	0.39	0.0	0	0.71	0.0	0	1.82	0.0
Trachea, bronchus, lung	3	3.12	1.0	3	5.21	0.6	3	4.67	0.6	5	8.83	0.6	14	21.82	0.6
Prostate gland	0	1.31	0.0	1	2.26	0.4	0	2.23	0.0	6	4.74	1.3	7	10.54	0.7
Testis	0	0.22	0.0	1	0.44	2.3	1	0.31	3.2	1	0.53	1.9	3	1.50	2.0
Kidney, renal pelvis, ureter	2	0.53	3.8	0	0.88	0.0	2	0.78	2.6	4	1.46	2.7	8	3.64	2.2
Bladder, other urinary	3	1.23	2.4	2	2.09	1.0	2	1.90	1.1	3	3.73	0.8	10	8.95	1.1
Melanoma of the skin	0	0.20	0.0	0	0.36	0.0	0	0.29	0.0	0	0.54	0.0	0	1.39	0.0
Eye	0	0.06	0.0	0	0.10	0.0	0	0.08	0.0	0	0.14	0.0	0	0.38	0.0
Brain, central nervous system	3	0.48	6.3[b]	1	0.82	1.2	1	0.63	1.6	2	1.01	2.0	7	2.94	2.4
Thyroid gland	0	0.05	0.0	0	0.09	0.0	0	0.07	0.0	0	0.13	0.0	0	0.35	0.0
Bone	0	0.04	0.0	1	0.08	12.5	0	0.06	0.0	0	0.09	0.0	1	0.28	3.6
Connective tissue	0	0.07	0.0	1	0.12	8.2	0	0.09	0.0	1	0.15	6.8	2	0.44	4.6
Lymphatic, hematopoietic system	**1**	**1.12**	**0.9**	**5**	**1.92**	**2.6**	**3**	**1.63**	**1.8**	**2**	**2.93**	**0.7**	**11**	**7.60**	**1.4**
Non-Hodgkin's lymphoma	0	0.30	0.0	2	0.52	3.8	0	0.45	0.0	0	0.81	0.0	2	2.08	1.0
Hodgkin's disease	0	0.14	0.0	0	0.26	0.0	0	0.20	0.0	0	0.31	0.0	0	0.90	0.0
Multiple myeloma	1	0.18	5.6	0	0.30	0.0	0	0.27	0.0	0	0.51	0.0	1	1.25	0.8
Leukemias	0	0.48	0.0	3	0.82	3.6	3	0.70	4.3	2	1.28	1.6	8	3.29	2.4[b]
Chronic lymphocytic	0	0.22	0.0	1	0.37	2.7	3	0.33	9.0[b]	1	0.62	1.6	5	1.55	3.2[b]
Acute nonlymphocytic	0	0.13	0.0	1	0.24	4.2	0	0.20	0.0	1	0.38	2.6	2	0.95	2.1

[a] ICD-7 code = 193.

[b] $P < .05$.

BRAIN
FEMALES

TABLE 3E *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the brain or central nervous system (including benign tumors) among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,013			2,943			1,720			1,153			5,013		
Person-yr in interval	3,784			8,676			7,039			10,747			30,246		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**14**	**16.99**	**0.8**	**40**	**38.82**	**1.0**	**44**	**37.06**	**1.2**	**95**	**75.79**	**1.3**[b]	**193**	**168.66**	**1.1**
All excluding site of initial cancer	**13**	**16.52**	**0.8**	**39**	**37.76**	**1.0**	**41**	**36.11**	**1.1**	**93**	**74.09**	**1.3**[b]	**186**	**164.49**	**1.1**
Buccal cavity, pharynx	**1**	**0.21**	**4.8**	**0**	**0.48**	**0.0**	**0**	**0.46**	**0.0**	**0**	**0.98**	**0.0**	**1**	**2.12**	**0.5**
Lip	0	0.03	0.0	0	0.07	0.0	0	0.07	0.0	0	0.15	0.0	0	0.31	0.0
Tongue	0	0.03	0.0	0	0.07	0.0	0	0.07	0.0	0	0.16	0.0	0	0.33	0.0
Salivary gland	1	0.06	17.3	0	0.13	0.0	0	0.12	0.0	0	0.20	0.0	1	0.51	2.0
Gum, other mouth	0	0.05	0.0	0	0.11	0.0	0	0.12	0.0	0	0.30	0.0	0	0.58	0.0
Pharynx	0	0.04	0.0	0	0.10	0.0	0	0.09	0.0	0	0.18	0.0	0	0.41	0.0
Digestive system	**2**	**4.45**	**0.4**	**4**	**10.00**	**0.4**	**16**	**10.26**	**1.6**	**20**	**23.40**	**0.9**	**42**	**48.11**	**0.9**
Esophagus	0	0.11	0.0	0	0.23	0.0	1	0.24	4.1	1	0.60	1.7	2	1.18	1.7
Stomach	0	0.98	0.0	0	2.11	0.0	2	2.16	0.9	6	4.63	1.3	8	9.88	0.8
Colon	1	1.44	0.7	1	3.30	0.3	5	3.40	1.5	4	8.06	0.5	11	16.19	0.7
Rectum	0	0.88	0.0	2	1.98	1.0	4	1.98	2.0	3	4.24	0.7	9	9.08	1.0
Liver, biliary	0	0.38	0.0	0	0.87	0.0	1	0.93	1.1	4	2.30	1.7	5	4.47	1.1
Pancreas	1	0.47	2.1	0	1.09	0.0	2	1.14	1.8	2	2.76	0.7	5	5.46	0.9
Respiratory system	**1**	**0.87**	**1.1**	**1**	**2.04**	**0.5**	**1**	**2.01**	**0.5**	**8**	**4.49**	**1.8**	**11**	**9.42**	**1.2**
Nasal cavities, sinuses	0	0.03	0.0	0	0.06	0.0	0	0.06	0.0	0	0.11	0.0	0	0.26	0.0
Larynx	0	0.04	0.0	1	0.10	10.3	0	0.09	0.0	0	0.19	0.0	1	0.42	2.4
Trachea, bronchus, lung	1	0.75	1.3	0	1.75	0.0	1	1.73	0.6	8	3.90	2.1	10	8.13	1.2
Female breast	1	3.99	0.3	11	9.18	1.2	4	8.47	0.5	17	16.54	1.0	33	38.17	0.9
Female genital tract	**4**	**4.28**	**0.9**	**9**	**9.82**	**0.9**	**9**	**8.78**	**1.0**	**18**	**15.33**	**1.2**	**40**	**38.21**	**1.0**
Cervix uteri	1	1.76	0.6	3	4.06	0.7	3	3.38	0.9	4	5.18	0.8	11	14.39	0.8
Corpus uteri	2	1.12	1.8	4	2.56	1.6	3	2.40	1.2	6	4.43	1.4	15	10.51	1.4
Uterus, NOS	0	0.06	0.0	0	0.13	0.0	0	0.12	0.0	0	0.22	0.0	0	0.53	0.0
Ovary, fallopian tubes	1	1.16	0.9	2	2.66	0.8	2	2.47	0.8	7	4.60	1.5	12	10.88	1.1
Kidney, renal pelvis, ureter	2	0.41	4.8	2	0.95	2.1	4	0.95	4.2[b]	10	2.08	4.8[b]	18	4.41	4.1[b]
Bladder, other urinary	0	0.40	0.0	1	0.92	1.1	1	0.95	1.0	3	2.25	1.3	5	4.52	1.1
Melanoma of the skin	0	0.31	0.0	3	0.72	4.2	2	0.65	3.1	6	1.34	4.5[b]	11	3.01	3.7[b]
Eye	0	0.05	0.0	0	0.12	0.0	0	0.11	0.0	0	0.21	0.0	0	0.50	0.0
Brain, central nervous system	1	0.47	2.1	1	1.06	0.9	3	0.95	3.2	2	1.70	1.2	7	4.17	1.7
Thyroid gland	1	0.11	9.1	3	0.25	11.9[b]	0	0.25	0.0	0	0.53	0.0	4	1.15	3.5
Bone	0	0.03	0.0	1	0.08	12.7	1	0.07	14.1	1	0.12	8.3	3	0.30	9.8[b]
Connective tissue	0	0.07	0.0	1	0.15	6.7	0	0.13	0.0	2	0.24	8.4	3	0.59	5.1[b]
Lymphatic, hematopoietic system	**1**	**0.86**	**1.2**	**3**	**1.98**	**1.5**	**2**	**1.96**	**1.0**	**3**	**4.24**	**0.7**	**9**	**9.05**	**1.0**
Non-Hodgkin's lymphoma	0	0.25	0.0	2	0.58	3.5	0	0.57	0.0	1	1.30	0.8	3	2.70	1.1
Hodgkin's disease	0	0.09	0.0	0	0.21	0.0	2	0.20	10.2[b]	0	0.34	0.0	2	0.84	2.4
Multiple myeloma	1	0.15	6.5	0	0.35	0.0	0	0.37	0.0	0	0.83	0.0	1	1.71	0.6
Leukemias	0	0.36	0.0	1	0.82	1.2	0	0.80	0.0	2	1.73	1.2	3	3.71	0.8
Chronic lymphocytic	0	0.13	0.0	1	0.28	3.5	0	0.30	0.0	1	0.71	1.4	2	1.41	1.4
Acute nonlymphocytic	0	0.12	0.0	0	0.28	0.0	0	0.27	0.0	1	0.61	1.6	1	1.28	0.8

[a] ICD-7 code = 193.

[b] $P < .05$.

THYROID
BOTH SEXES

TABLE 4A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the thyroid gland, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	584	1,351	1,935
No. who developed a second primary cancer	28	50	78
Average age at diagnosis of first cancer, yr	58	59	59
Average yr of diagnosis of first cancer	1966	1965	1965
Person-yr of follow-up	2,766	7,994	10,760
Average follow-up, yr	4.7	5.9	5.6
Percent given radiotherapy for first cancer	54	49	50

[a] ICD-7 code = 194.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the thyroid gland in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	64	82.1
Only the first cancer	10	12.8
Only the second cancer	4	5.1
Neither first nor second cancer	0	0.0
Total second primary cancers	78	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

THYROID
BOTH SEXES

TABLE 4C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the thyroid gland among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,935			1,201			696			419			1,935		
Person-yr in interval	1,494			3,562			2,663			3,041			10,760		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**12**	**11.31**	**1.1**	**24**	**24.79**	**1.0**	**24**	**19.43**	**1.2**	**18**	**25.43**	**0.7**	**78**	**80.95**	**1.0**
All excluding site of initial cancer	**12**	**11.25**	**1.1**	**24**	**24.64**	**1.0**	**24**	**19.31**	**1.2**	**18**	**25.28**	**0.7**	**78**	**80.47**	**1.0**
Buccal cavity, pharynx	**0**	**0.23**	**0.0**	**0**	**0.48**	**0.0**	**1**	**0.35**	**2.9**	**1**	**0.43**	**2.3**	**2**	**1.50**	**1.3**
Lip	0	0.08	0.0	0	0.18	0.0	0	0.12	0.0	1	0.14	7.1	1	0.52	1.9
Tongue	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.18	0.0
Salivary gland	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Gum, other mouth	0	0.05	0.0	0	0.10	0.0	1	0.07	14.3	0	0.11	0.0	1	0.33	3.0
Pharynx	0	0.04	0.0	0	0.08	0.0	0	0.06	0.0	0	0.08	0.0	0	0.25	0.0
Digestive system	**4**	**3.97**	**1.0**	**12**	**8.25**	**1.5**	**11**	**6.38**	**1.7**	**2**	**8.00**	**0.3**[b]	**29**	**26.61**	**1.1**
Esophagus	0	0.13	0.0	0	0.27	0.0	1	0.20	5.0	0	0.24	0.0	1	0.84	1.2
Stomach	1	1.13	0.9	0	2.18	0.0	4	1.57	2.5	0	1.69	0.0	5	6.56	0.8
Colon	1	1.09	0.9	7	2.36	3.0[b]	3	1.93	1.6	1	2.60	0.4	12	7.99	1.5
Rectum	2	0.77	2.6	3	1.61	1.9	0	1.22	0.0	0	1.53	0.0	5	5.13	1.0
Liver, biliary	0	0.29	0.0	1	0.64	1.6	2	0.53	3.8	1	0.73	1.4	4	2.18	1.8
Pancreas	0	0.40	0.0	1	0.88	1.1	0	0.70	0.0	0	0.96	0.0	1	2.95	0.3
Respiratory system	**0**	**1.18**	**0.0**	**0**	**2.65**	**0.0**	**2**	**1.96**	**1.0**	**2**	**2.63**	**0.8**	**4**	**8.42**	**0.5**
Nasal cavities, sinuses	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.05	0.0	0	0.15	0.0
Larynx	0	0.08	0.0	0	0.17	0.0	1	0.11	9.1	0	0.15	0.0	1	0.49	2.0
Trachea, bronchus, lung	0	1.02	0.0	0	2.30	0.0	1	1.70	0.6	2	2.31	0.9	3	7.32	0.4
Female breast	1	1.55	0.6	4	3.56	1.1	1	3.03	0.3	5	4.30	1.2	11	12.45	0.9
Female genital tract	**1**	**1.45**	**0.7**	**2**	**3.40**	**0.6**	**2**	**2.80**	**0.7**	**2**	**3.77**	**0.5**	**7**	**11.43**	**0.6**
Cervix uteri	0	0.51	0.0	2	1.26	1.6	2	1.03	1.9	1	1.24	0.8	5	4.04	1.2
Corpus uteri	1	0.39	2.5	0	0.90	0.0	0	0.75	0.0	0	1.10	0.0	1	3.15	0.3
Uterus, NOS	0	0.03	0.0	0	0.06	0.0	0	0.05	0.0	0	0.06	0.0	0	0.20	0.0
Ovary, fallopian tubes	0	0.42	0.0	0	0.98	0.0	0	0.81	0.0	1	1.14	0.9	1	3.35	0.3
Prostate gland	0	0.49	0.0	1	1.06	0.9	1	0.72	1.4	1	0.81	1.2	3	3.07	1.0
Testis	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.18	0.0
Kidney, renal pelvis, ureter	0	0.32	0.0	1	0.70	1.4	2	0.55	3.6	1	0.74	1.4	4	2.33	1.7
Bladder, other urinary	0	0.51	0.0	1	1.14	0.9	0	0.86	0.0	0	1.14	0.0	1	3.66	0.3
Melanoma of the skin	0	0.14	0.0	0	0.35	0.0	0	0.29	0.0	0	0.41	0.0	0	1.19	0.0
Eye	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.07	0.0	0	0.23	0.0
Brain, central nervous system	2	0.23	8.7	1	0.52	1.9	0	0.40	0.0	2	0.54	3.7	5	1.67	3.0
Thyroid gland	0	0.06	0.0	0	0.15	0.0	0	0.12	0.0	0	0.15	0.0	0	0.48	0.0
Bone	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.04	0.0	0	0.14	0.0
Connective tissue	1	0.04	25.0	0	0.09	0.0	0	0.06	0.0	0	0.08	0.0	1	0.26	3.8
Lymphatic, hematopoietic system	**3**	**0.65**	**4.6**	**2**	**1.44**	**1.4**	**4**	**1.13**	**3.5**	**0**	**1.47**	**0.0**	**9**	**4.69**	**1.9**
Non-Hodgkin's lymphoma	3	0.18	16.7[b]	1	0.41	2.4	2	0.32	6.3	0	0.44	0.0	6	1.35	4.4[b]
Hodgkin's disease	0	0.05	0.0	0	0.13	0.0	0	0.09	0.0	0	0.11	0.0	0	0.39	0.0
Multiple myeloma	0	0.13	0.0	0	0.27	0.0	0	0.22	0.0	0	0.29	0.0	0	0.90	0.0
Leukemias	0	0.28	0.0	1	0.62	1.6	2	0.48	4.2	0	0.63	0.0	3	0.80	1.5
Chronic lymphocytic	0	0.14	0.0	0	0.29	0.0	1	0.22	4.5	0	0.28	0.0	1	0.93	1.1
Acute nonlymphocytic	0	0.08	0.0	0	0.17	0.0	1	0.14	7.1	0	0.21	0.0	1	0.60	1.7

[a] ICD-7 code = 194.

[b] $P < .05$.

THYROID
MALES

TABLE 4D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the thyroid gland among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	584			364			188			98			584		
Person-yr in interval	454			1,034			662			616			2,766		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**3.89**	**0.5**	**9**	**8.35**	**1.1**	**10**	**5.52**	**1.8**	**7**	**6.09**	**1.1**	**28**	**23.85**	**1.2**
All excluding site of initial cancer	**2**	**3.88**	**0.5**	**9**	**8.32**	**1.1**	**10**	**5.50**	**1.8**	**7**	**6.07**	**1.2**	**28**	**23.77**	**1.2**
Buccal cavity, pharynx	**0**	**0.13**	**0.0**	**0**	**0.27**	**0.0**	**0**	**0.17**	**0.0**	**1**	**0.18**	**5.5**	**1**	**0.76**	**1.3**
Lip	0	0.07	0.0	0	0.15	0.0	0	0.09	0.0	1	0.10	10.5	1	0.41	2.5
Tongue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Gum, other mouth	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.03	0.0	0	0.11	0.0
Pharynx	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.03	0.0	0	0.12	0.0
Digestive system	**1**	**1.44**	**0.7**	**6**	**2.97**	**2.0**	**5**	**1.93**	**2.6**	**0**	**1.99**	**0.0**	**12**	**8.34**	**1.4**
Esophagus	0	0.06	0.0	0	0.13	0.0	0	0.08	0.0	0	0.08	0.0	0	0.35	0.0
Stomach	0	0.46	0.0	0	0.88	0.0	2	0.56	3.6	0	0.51	0.0	2	2.40	0.8
Colon	1	0.32	3.1	5	0.69	7.2[b]	2	0.46	4.3	0	0.51	0.0	8	1.99	4.0[b]
Rectum	0	0.32	0.0	1	0.67	1.5	0	0.43	0.0	0	0.45	0.0	1	1.87	0.5
Liver, biliary	0	0.08	0.0	0	0.17	0.0	0	0.12	0.0	0	0.14	0.0	0	0.50	0.0
Pancreas	0	0.15	0.0	0	0.33	0.0	0	0.22	0.0	0	0.25	0.0	0	0.96	0.0
Respiratory system	**0**	**0.82**	**0.0**	**0**	**1.81**	**0.0**	**2**	**1.21**	**1.6**	**1**	**1.45**	**0.7**	**3**	**5.29**	**0.6**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Larynx	0	0.06	0.0	0	0.13	0.0	1	0.08	12.1	0	0.10	0.0	1	0.36	2.7
Trachea, bronchus, lung	0	0.71	0.0	0	1.59	0.0	1	1.06	0.9	1	1.28	0.8	2	4.64	0.4
Prostate gland	0	0.49	0.0	1	1.06	0.9	1	0.72	1.4	1	0.81	1.2	3	3.07	1.0
Testis	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.18	0.0
Kidney, renal pelvis, ureter	0	0.13	0.0	0	0.28	0.0	1	0.19	5.2	1	0.21	4.7	2	0.82	2.5
Bladder, other urinary	0	0.31	0.0	0	0.70	0.0	0	0.47	0.0	0	0.56	0.0	0	2.05	0.0
Melanoma of the skin	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.24	0.0
Eye	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Brain, central nervous system	0	0.08	0.0	1	0.17	5.9	0	0.11	0.0	1	0.12	8.5	2	0.47	4.2
Thyroid gland	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Connective tissue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Lymphatic, hematopoietic system	**1**	**0.26**	**3.8**	**1**	**0.57**	**1.8**	**1**	**0.38**	**2.6**	**0**	**0.41**	**0.0**	**3**	**1.62**	**1.9**
Non-Hodgkin's lymphoma	1	0.07	14.7	1	0.15	6.7	0	0.10	0.0	0	0.11	0.0	2	0.43	4.7
Hodgkin's disease	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.14	0.0
Multiple myeloma	0	0.05	0.0	0	0.10	0.0	0	0.07	0.0	0	0.08	0.0	0	0.30	0.0
Leukemias	0	0.12	0.0	0	0.26	0.0	1	0.17	5.8	0	0.19	0.0	1	0.74	1.4
Chronic lymphocytic	0	0.07	0.0	0	0.14	0.0	1	0.09	10.8	0	0.10	0.0	1	0.40	2.5
Acute nonlymphocytic	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.05	0.0	0	0.19	0.0

[a] ICD-7 code = 194.

[b] $P < .05$.

THYROID
FEMALES

TABLE 4E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the thyroid gland among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,351			837			508			321			1,351		
Person-yr in interval	1,040			2,528			2,001			2,425			7,994		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**10**	**7.42**	**1.3**	**15**	**16.44**	**0.9**	**14**	**13.91**	**1.0**	**11**	**19.34**	**0.6**	**50**	**57.10**	**0.9**
All excluding site of initial cancer	**10**	**7.37**	**1.4**	**15**	**16.32**	**0.9**	**14**	**13.81**	**1.0**	**11**	**19.21**	**0.6**	**50**	**56.70**	**0.9**
Buccal cavity, pharynx	**0**	**0.10**	**0.0**	**0**	**0.21**	**0.0**	**1**	**0.18**	**5.6**	**0**	**0.25**	**0.0**	**1**	**0.74**	**1.3**
Lip	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.04	0.0	0	0.11	0.0
Tongue	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.04	0.0	0	0.13	0.0
Salivary gland	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.04	0.0	0	0.16	0.0
Gum, other mouth	0	0.03	0.0	0	0.06	0.0	1	0.05	19.4	0	0.08	0.0	1	0.22	4.6
Pharynx	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.13	0.0
Digestive system	**3**	**2.53**	**1.2**	**6**	**5.28**	**1.1**	**6**	**4.45**	**1.3**	**2**	**6.01**	**0.3**	**17**	**18.27**	**0.9**
Esophagus	0	0.07	0.0	0	0.14	0.0	1	0.12	8.3	0	0.16	0.0	1	0.49	2.0
Stomach	1	0.67	1.5	0	1.30	0.0	2	1.01	2.0	0	1.18	0.0	3	4.16	0.7
Colon	0	0.77	0.0	2	1.67	1.2	1	1.47	0.7	1	2.09	0.5	4	6.00	0.7
Rectum	2	0.45	4.5	2	0.94	2.1	0	0.79	0.0	0	1.08	0.0	4	3.26	1.2
Liver, biliary	0	0.21	0.0	1	0.47	2.1	2	0.41	4.8	1	0.59	1.7	4	1.68	2.4
Pancreas	0	0.25	0.0	1	0.55	1.8	0	0.48	0.0	0	0.71	0.0	1	1.99	0.5
Respiratory system	**0**	**0.36**	**0.0**	**0**	**0.84**	**0.0**	**0**	**0.75**	**0.0**	**1**	**1.18**	**0.8**	**1**	**3.13**	**0.3**
Nasal cavities, sinuses	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Larynx	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.13	0.0
Trachea, bronchus, lung	0	0.31	0.0	0	0.71	0.0	0	0.64	0.0	1	1.03	1.0	1	2.68	0.4
Female breast	1	1.55	0.6	4	3.56	1.1	1	3.03	0.3	5	4.30	1.2	11	12.45	0.9
Female genital tract	**1**	**1.45**	**0.7**	**2**	**3.40**	**0.6**	**2**	**2.80**	**0.7**	**2**	**3.77**	**0.5**	**7**	**11.43**	**0.6**
Cervix uteri	0	0.51	0.0	2	1.26	1.6	2	1.03	1.9	1	1.24	0.8	5	4.04	1.2
Corpus uteri	1	0.39	2.5	0	0.90	0.0	0	0.75	0.0	0	1.10	0.0	1	3.15	0.3
Uterus, NOS	0	0.03	0.0	0	0.06	0.0	0	0.05	0.0	0	0.06	0.0	0	0.20	0.0
Ovary, fallopian tubes	0	0.42	0.0	0	0.98	0.0	0	0.81	0.0	1	1.14	0.9	1	3.35	0.3
Kidney, renal pelvis, ureter	0	0.19	0.0	1	0.42	2.4	1	0.36	2.7	0	0.53	0.0	2	1.51	1.3
Bladder, other urinary	0	0.20	0.0	1	0.44	2.3	0	0.39	0.0	0	0.58	0.0	1	1.61	0.6
Melanoma of the skin	0	0.10	0.0	0	0.26	0.0	0	0.23	0.0	0	0.35	0.0	0	0.95	0.0
Eye	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.05	0.0	0	0.16	0.0
Brain, central nervous system	2	0.15	13.8[b]	0	0.35	0.0	0	0.29	0.0	1	0.42	2.4	3	1.20	2.5
Thyroid gland	0	0.05	0.0	0	0.12	0.0	0	0.10	0.0	0	0.13	0.0	0	0.40	0.0
Bone	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Connective tissue	1	0.03	38.4	0	0.06	0.0	0	0.04	0.0	0	0.06	0.0	1	0.18	5.4
Lymphatic, hematopoietic system	**2**	**0.39**	**5.1**	**1**	**0.87**	**1.1**	**3**	**0.75**	**4.0**	**0**	**1.06**	**0.0**	**6**	**3.07**	**2.0**
Non-Hodgkin's lymphoma	2	0.11	17.6[b]	0	0.26	0.0	2	0.22	8.9[b]	0	0.33	0.0	4	0.92	4.3[b]
Hodgkin's disease	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.08	0.0	0	0.25	0.0
Multiple myeloma	0	0.08	0.0	0	0.17	0.0	0	0.15	0.0	0	0.21	0.0	0	0.60	0.0
Leukemias	0	0.16	0.0	1	0.36	2.8	1	0.31	3.2	0	0.44	0.0	2	1.27	1.6
Chronic lymphocytic	0	0.07	0.0	0	0.15	0.0	0	0.13	0.0	0	0.18	0.0	0	0.53	0.0
Acute nonlymphocytic	0	0.05	0.0	0	0.11	0.0	1	0.10	10.0	0	0.16	0.0	1	0.41	2.4

[a] ICD-7 code = 194.

[b] $P < .05$.

BONE
BOTH SEXES

TABLE 5A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the bone, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	889	653	1,542
No. who developed a second primary cancer	21	23	44
Average age at diagnosis of first cancer, yr	41	44	42
Average yr of diagnosis of first cancer	1963	1962	1963
Person-yr of follow-up	4,935	3,713	8,648
Average follow-up, yr	5.6	5.7	5.6
Percent given radiotherapy for first cancer	47	45	46

[a] ICD-7 code = 196.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 5B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the bone in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	33	75.0
Only the first cancer	3	6.8
Only the second cancer	6	13.6
Neither first nor second cancer	2	4.6
Total second primary cancers	44	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

BONE
BOTH SEXES

TABLE 5C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bone among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,542			996			454			292			1,542		
Person-yr in interval	1,261			2,482			1,853			3,052			8,648		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**5.91**	**0.3**	**11**	**12.07**	**0.9**	**9**	**9.57**	**0.9**	**22**	**19.93**	**1.1**	**44**	**47.47**	**0.9**
All excluding site of initial cancer	**2**	**5.89**	**0.3**	**11**	**12.04**	**0.9**	**9**	**9.55**	**0.9**	**22**	**19.89**	**1.1**	**44**	**47.36**	**0.9**
Buccal cavity, pharynx	**0**	**0.15**	**0.0**	**0**	**0.31**	**0.0**	**0**	**0.23**	**0.0**	**0**	**0.47**	**0.0**	**0**	**1.16**	**0.0**
Lip	0	0.07	0.0	0	0.14	0.0	0	0.11	0.0	0	0.21	0.0	0	0.52	0.0
Tongue	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.04	0.0	0	0.11	0.0
Salivary gland	0	0.02	0.0	0	0.04	0.0	0	0.04	0.0	0	0.06	0.0	0	0.15	0.0
Gum, other mouth	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.09	0.0	0	0.20	0.0
Pharynx	0	0.03	0.0	0	0.05	0.0	0	0.04	0.0	0	0.08	0.0	0	0.19	0.0
Digestive system	**1**	**2.14**	**0.5**	**5**	**4.19**	**1.2**	**1**	**3.26**	**0.3**	**2**	**6.59**	**0.3**	**9**	**16.18**	**0.6**
Esophagus	0	0.08	0.0	0	0.15	0.0	0	0.11	0.0	0	0.24	0.0	0	0.58	0.0
Stomach	1	0.67	1.5	2	1.22	1.6	0	0.92	0.0	2	1.67	1.2	5	4.48	1.1
Colon	0	0.53	0.0	0	1.09	0.0	1	0.88	1.1	0	1.87	0.0	1	4.38	0.2
Rectum	0	0.44	0.0	3	0.87	3.4	0	0.66	0.0	0	1.33	0.0	3	3.30	0.9
Liver, biliary	0	0.14	0.0	0	0.27	0.0	0	0.22	0.0	0	0.51	0.0	0	1.14	0.0
Pancreas	0	0.21	0.0	0	0.43	0.0	0	0.34	0.0	0	0.76	0.0	0	1.73	0.0
Respiratory system	**0**	**0.76**	**0.0**	**1**	**1.63**	**0.6**	**2**	**1.26**	**1.6**	**6**	**2.95**	**2.0**	**9**	**6.59**	**1.4**
Nasal cavities, sinuses	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.04	0.0	0	0.11	0.0
Larynx	0	0.05	0.0	0	0.11	0.0	0	0.09	0.0	0	0.19	0.0	0	0.43	0.0
Trachea, bronchus, lung	0	0.65	0.0	1	1.41	0.7	2	1.08	1.9	6	2.58	2.3	9	5.72	1.6
Female breast	0	0.51	0.0	0	1.05	0.0	3	0.94	3.2	3	1.99	1.5	6	4.50	1.3
Female genital tract	**0**	**0.50**	**0.0**	**0**	**1.05**	**0.0**	**1**	**0.93**	**1.1**	**2**	**1.77**	**1.1**	**3**	**4.26**	**0.7**
Cervix uteri	0	0.19	0.0	0	0.40	0.0	0	0.34	0.0	0	0.63	0.0	0	1.56	0.0
Corpus uteri	0	0.13	0.0	0	0.28	0.0	0	0.25	0.0	1	0.47	2.1	1	1.13	0.9
Uterus, NOS	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Ovary, fallopian tubes	0	0.14	0.0	0	0.30	0.0	1	0.26	3.8	1	0.52	1.9	2	1.22	1.6
Prostate gland	0	0.45	0.0	0	0.92	0.0	0	0.63	0.0	1	1.26	0.8	1	3.25	0.3
Testis	0	0.04	0.0	1	0.09	11.2	0	0.07	0.0	1	0.14	7.1	2	0.34	5.9
Kidney, renal pelvis, ureter	0	0.17	0.0	0	0.36	0.0	1	0.28	3.6	4	0.62	6.5[b]	5	1.43	3.5[b]
Bladder, other urinary	0	0.32	0.0	1	0.69	1.4	0	0.53	0.0	1	1.19	0.8	2	2.73	0.7
Melanoma of the skin	0	0.06	0.0	0	0.15	0.0	0	0.13	0.0	0	0.30	0.0	0	0.64	0.0
Eye	0	0.02	0.0	1	0.03	33.3	1	0.03	33.3	1	0.07	14.3	3	0.15	20.0[b]
Brain, central nervous system	0	0.12	0.0	1	0.27	3.7	0	0.22	0.0	1	0.44	2.3	2	1.06	1.9
Thyroid gland	1	0.03	33.3	0	0.05	0.0	0	0.05	0.0	0	0.10	0.0	1	0.23	4.3
Bone	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.04	0.0	0	0.11	0.0
Connective tissue	0	0.03	0.0	0	0.05	0.0	0	0.04	0.0	0	0.07	0.0	0	0.18	0.0
Lymphatic, hematopoietic system	**0**	**0.38**	**0.0**	**1**	**0.78**	**1.3**	**0**	**0.62**	**0.0**	**0**	**1.28**	**0.0**	**1**	**3.06**	**0.3**
Non-Hodgkin's lymphoma	0	0.10	0.0	0	0.20	0.0	0	0.17	0.0	0	0.35	0.0	0	0.83	0.0
Hodgkin's disease	0	0.04	0.0	1	0.09	11.1	0	0.06	0.0	0	0.12	0.0	1	0.32	3.1
Multiple myeloma	0	0.06	0.0	0	0.14	0.0	0	0.10	0.0	0	0.23	0.0	0	0.54	0.0
Leukemias	0	0.18	0.0	0	0.35	0.0	0	0.27	0.0	0	0.55	0.0	0	1.34	0.0
Chronic lymphocytic	0	0.08	0.0	0	0.17	0.0	0	0.12	0.0	0	0.26	0.0	0	0.64	0.0
Acute nonlymphocytic	0	0.05	0.0	0	0.09	0.0	0	0.07	0.0	0	0.16	0.0	0	0.37	0.0

[a] ICD-7 code = 196.

[b] $P < .05$.

BONE
MALES

TABLE 5D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bone among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	889			582			258			163			889		
Person-yr in interval	738			1,457			1,037			1,703			4,935		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**0**	**3.49**	**0.0**	**9**	**7.14**	**1.3**	**3**	**5.06**	**0.6**	**9**	**10.62**	**0.8**	**21**	**26.30**	**0.8**
All excluding site of initial cancer	**0**	**3.48**	**0.0**	**9**	**7.12**	**1.3**	**3**	**5.05**	**0.6**	**9**	**10.60**	**0.8**	**21**	**26.23**	**0.8**
Buccal cavity, pharynx	**0**	**0.12**	**0.0**	**0**	**0.24**	**0.0**	**0**	**0.17**	**0.0**	**0**	**0.35**	**0.0**	**0**	**0.88**	**0.0**
Lip	0	0.07	0.0	0	0.13	0.0	0	0.10	0.0	0	0.19	0.0	0	0.48	0.0
Tongue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.06	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Gum, other mouth	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.05	0.0	0	0.12	0.0
Pharynx	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.06	0.0	0	0.14	0.0
Digestive system	**0**	**1.34**	**0.0**	**5**	**2.59**	**1.9**	**0**	**1.78**	**0.0**	**2**	**3.52**	**0.6**	**7**	**9.23**	**0.8**
Esophagus	0	0.06	0.0	0	0.11	0.0	0	0.07	0.0	0	0.15	0.0	0	0.39	0.0
Stomach	0	0.45	0.0	2	0.80	2.5	0	0.54	0.0	2	0.96	2.1	4	2.75	1.5
Colon	0	0.29	0.0	0	0.60	0.0	0	0.42	0.0	0	0.86	0.0	0	2.18	0.0
Rectum	0	0.30	0.0	3	0.58	5.2[b]	0	0.40	0.0	0	0.79	0.0	3	2.07	1.4
Liver, biliary	0	0.07	0.0	0	0.14	0.0	0	0.10	0.0	0	0.22	0.0	0	0.53	0.0
Pancreas	0	0.13	0.0	0	0.28	0.0	0	0.19	0.0	0	0.42	0.0	0	1.02	0.0
Respiratory system	**0**	**0.65**	**0.0**	**1**	**1.40**	**0.7**	**2**	**1.04**	**1.9**	**2**	**2.45**	**0.8**	**5**	**5.54**	**0.9**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Larynx	0	0.05	0.0	0	0.10	0.0	0	0.08	0.0	0	0.17	0.0	0	0.39	0.0
Trachea, bronchus, lung	0	0.56	0.0	1	1.22	0.8	2	0.90	2.2	2	2.15	0.9	5	4.83	1.0
Prostate gland	0	0.45	0.0	0	0.92	0.0	0	0.63	0.0	1	1.26	0.8	1	3.25	0.3
Testis	0	0.04	0.0	1	0.09	11.2	0	0.07	0.0	1	0.14	7.1	2	0.34	5.9
Kidney, renal pelvis, ureter	0	0.11	0.0	0	0.24	0.0	0	0.17	0.0	2	0.37	5.3	2	0.89	2.2
Bladder, other urinary	0	0.26	0.0	1	0.57	1.8	0	0.41	0.0	1	0.92	1.1	2	2.16	0.9
Melanoma of the skin	0	0.03	0.0	0	0.08	0.0	0	0.06	0.0	0	0.14	0.0	0	0.31	0.0
Eye	0	0.01	0.0	0	0.02	0.0	1	0.02	59.5	0	0.04	0.0	1	0.09	11.3
Brain, central nervous system	0	0.07	0.0	1	0.16	6.2	0	0.12	0.0	0	0.25	0.0	1	0.61	1.6
Thyroid gland	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.08	0.0
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.02	0.0	0	0.07	0.0
Connective tissue	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.04	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**0**	**0.25**	**0.0**	**0**	**0.52**	**0.0**	**0**	**0.38**	**0.0**	**0**	**0.76**	**0.0**	**0**	**1.91**	**0.0**
Non-Hodgkin's lymphoma	0	0.06	0.0	0	0.13	0.0	0	0.10	0.0	0	0.20	0.0	0	0.50	0.0
Hodgkin's disease	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.08	0.0	0	0.21	0.0
Multiple myeloma	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.13	0.0	0	0.32	0.0
Leukemias	0	0.12	0.0	0	0.24	0.0	0	0.17	0.0	0	0.34	0.0	0	0.86	0.0
Chronic lymphocytic	0	0.06	0.0	0	0.12	0.0	0	0.08	0.0	0	0.17	0.0	0	0.44	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.09	0.0	0	0.23	0.0

[a] ICD-7 code = 196.
[b] $P < .05$.

BONE
FEMALES

TABLE 5E. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the bone among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	653			414			196			129			653		
Person-yr in interval	523			1,024			816			1,350			3,713		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**2**	**2.42**	**0.8**	**2**	**4.93**	**0.4**	**6**	**4.51**	**1.3**	**13**	**9.31**	**1.4**	**23**	**21.17**	**1.1**
All excluding site of initial cancer	**2**	**2.41**	**0.8**	**2**	**4.92**	**0.4**	**6**	**4.50**	**1.3**	**13**	**9.29**	**1.4**	**23**	**21.13**	**1.1**
Buccal cavity, pharynx	**0**	**0.03**	**0.0**	**0**	**0.07**	**0.0**	**0**	**0.06**	**0.0**	**0**	**0.12**	**0.0**	**0**	**0.28**	**0.0**
Lip	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Tongue	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Salivary gland	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.07	0.0
Gum, other mouth	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.08	0.0
Pharynx	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.05	0.0
Digestive system	**1**	**0.80**	**1.2**	**0**	**1.60**	**0.0**	**1**	**1.48**	**0.7**	**0**	**3.07**	**0.0**	**2**	**6.95**	**0.3**
Esophagus	0	0.02	0.0	0	0.04	0.0	0	0.04	0.0	0	0.09	0.0	0	0.19	0.0
Stomach	1	0.22	4.5	0	0.42	0.0	0	0.38	0.0	0	0.71	0.0	1	1.73	0.6
Colon	0	0.24	0.0	0	0.49	0.0	1	0.46	2.2	0	1.01	0.0	1	2.20	0.5
Rectum	0	0.14	0.0	0	0.29	0.0	0	0.26	0.0	0	0.54	0.0	0	1.23	0.0
Liver, biliary	0	0.07	0.0	0	0.13	0.0	0	0.12	0.0	0	0.29	0.0	0	0.61	0.0
Pancreas	0	0.08	0.0	0	0.15	0.0	0	0.15	0.0	0	0.34	0.0	0	0.71	0.0
Respiratory system	**0**	**0.11**	**0.0**	**0**	**0.23**	**0.0**	**0**	**0.22**	**0.0**	**4**	**0.50**	**8.0**[b]	**4**	**1.05**	**3.8**[b]
Nasal cavities, sinuses	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.03	0.0
Larynx	0	0.00	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Trachea, bronchus, lung	0	0.09	0.0	0	0.19	0.0	0	0.18	0.0	4	0.43	9.4[b]	4	0.89	4.5[b]
Female breast	0	0.51	0.0	0	1.05	0.0	3	0.94	3.2	3	1.99	1.5	6	4.50	1.3
Female genital tract	**0**	**0.50**	**0.0**	**0**	**1.05**	**0.0**	**1**	**0.93**	**1.1**	**2**	**1.77**	**1.1**	**3**	**4.26**	**0.7**
Cervix uteri	0	0.19	0.0	0	0.40	0.0	0	0.34	0.0	0	0.63	0.0	0	1.56	0.0
Corpus uteri	0	0.13	0.0	0	0.28	0.0	0	0.25	0.0	1	0.47	2.1	1	1.13	0.9
Uterus, NOS	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.09	0.0
Ovary, fallopian tubes	0	0.14	0.0	0	0.30	0.0	1	0.26	3.8	1	0.52	1.9	2	1.22	1.6
Kidney, renal pelvis, ureter	0	0.06	0.0	0	0.12	0.0	1	0.11	8.7	2	0.25	8.1	3	0.54	5.6[b]
Bladder, other urinary	0	0.06	0.0	0	0.12	0.0	0	0.12	0.0	0	0.27	0.0	0	0.57	0.0
Melanoma of the skin	0	0.03	0.0	0	0.07	0.0	0	0.07	0.0	0	0.16	0.0	0	0.33	0.0
Eye	0	0.01	0.0	1	0.01	66.8[b]	0	0.01	0.0	1	0.03	39.4	2	0.06	32.6[b]
Brain, central nervous system	0	0.05	0.0	0	0.11	0.0	0	0.10	0.0	1	0.19	5.3	1	0.45	2.2
Thyroid gland	1	0.02	59.5	0	0.03	0.0	0	0.03	0.0	0	0.07	0.0	1	0.15	6.5
Bone	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.02	0.0	0	0.04	0.0
Connective tissue	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.03	0.0	0	0.07	0.0
Lymphatic, hematopoietic system	**0**	**0.13**	**0.0**	**1**	**0.26**	**3.8**	**0**	**0.24**	**0.0**	**0**	**0.52**	**0.0**	**1**	**1.15**	**0.9**
Non-Hodgkin's lymphoma	0	0.04	0.0	0	0.07	0.0	0	0.07	0.0	0	0.15	0.0	0	0.33	0.0
Hodgkin's disease	0	0.01	0.0	1	0.03	36.1	0	0.02	0.0	0	0.04	0.0	1	0.11	9.2
Multiple myeloma	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.10	0.0	0	0.22	0.0
Leukemias	0	0.06	0.0	0	0.11	0.0	0	0.10	0.0	0	0.21	0.0	0	0.48	0.0
Chronic lymphocytic	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.09	0.0	0	0.20	0.0
Acute nonlymphocytic	0	0.02	0.0	0	0.03	0.0	0	0.03	0.0	0	0.07	0.0	0	0.14	0.0

[a] ICD-7 code = 196.

[b] $P < .05$.

CONNECTIVE
BOTH SEXES

TABLE 6A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial cancer of the connective tissue, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,224	1,094	2,318
No. who developed a second primary cancer	60	63	123
Average age at diagnosis of first cancer, yr	53	52	52
Average yr of diagnosis of first cancer	1962	1961	1961
Person-yr of follow-up	8,040	9,325	17,365
Average follow-up, yr	6.6	8.5	7.6
Percent given radiotherapy for first cancer	42	39	41

[a] ICD-7 code = 197.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 6B.—*Microscopic confirmation among persons who developed second primary cancers after an initial cancer of the connective tissue in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	86	69.9
Only the first cancer	25	20.3
Only the second cancer	10	8.1
Neither first nor second cancer	2	1.6
Total second primary cancers	123	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

CONNECTIVE
BOTH SEXES

TABLE 6C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the connective tissue among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,318			1,664			934			619			2,318		
Person-yr in interval	1,974			4,756			3,770			6,866			17,365		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**9**	**13.21**	**0.7**	**23**	**30.35**	**0.8**	**24**	**24.04**	**1.0**	**67**	**54.88**	**1.2**	**123**	**122.47**	**1.0**
All excluding site of initial cancer	**9**	**13.15**	**0.7**	**23**	**30.23**	**0.8**	**24**	**23.95**	**1.0**	**67**	**54.71**	**1.2**	**123**	**122.02**	**1.0**
Buccal cavity, pharynx	**0**	**0.34**	**0.0**	**0**	**0.75**	**0.0**	**1**	**0.56**	**1.8**	**1**	**1.17**	**0.9**	**2**	**2.83**	**0.7**
Lip	0	0.16	0.0	0	0.35	0.0	1	0.25	4.0	1	0.48	2.1	2	1.23	1.6
Tongue	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.12	0.0	0	0.28	0.0
Salivary gland	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	0	0.15	0.0	0	0.36	0.0
Gum, other mouth	0	0.05	0.0	0	0.11	0.0	0	0.09	0.0	0	0.24	0.0	0	0.50	0.0
Pharynx	0	0.05	0.0	0	0.12	0.0	0	0.09	0.0	0	0.20	0.0	0	0.46	0.0
Digestive system	**3**	**4.94**	**0.6**	**4**	**10.77**	**0.4^b**	**3**	**8.16**	**0.4**	**22**	**17.62**	**1.2**	**32**	**41.50**	**0.8**
Esophagus	0	0.20	0.0	0	0.42	0.0	0	0.30	0.0	0	0.59	0.0	0	1.51	0.0
Stomach	3	1.59	1.9	2	3.30	0.6	1	2.36	0.4	3	4.11	0.7	9	11.36	0.8
Colon	0	1.21	0.0	1	2.73	0.4	1	2.16	0.5	9	5.24	1.7	11	11.34	1.0
Rectum	0	1.01	0.0	0	2.22	0.0	0	1.68	0.0	5	3.58	1.4	5	8.49	0.6
Liver, biliary	0	0.29	0.0	0	0.67	0.0	0	0.54	0.0	2	1.44	1.4	2	2.93	0.7
Pancreas	0	0.44	0.0	0	1.02	0.0	1	0.82	1.2	2	2.09	1.0	3	4.38	0.7
Respiratory system	**2**	**1.63**	**1.2**	**7**	**3.80**	**1.8**	**3**	**3.01**	**1.0**	**10**	**7.56**	**1.3**	**22**	**16.00**	**1.4**
Nasal cavities, sinuses	0	0.03	0.0	0	0.07	0.0	0	0.06	0.0	0	0.11	0.0	0	0.27	0.0
Larynx	0	0.11	0.0	0	0.26	0.0	0	0.19	0.0	1	0.48	2.1	1	1.05	1.0
Trachea, bronchus, lung	2	1.40	1.4	6	3.28	1.8	3	2.60	1.2	8	6.63	1.2	19	13.91	1.4
Female breast	0	1.19	0.0	2	3.01	0.7	7	2.60	2.7^b	11	6.52	1.7	20	13.33	1.5
Female genital tract	**1**	**1.16**	**0.9**	**0**	**3.04**	**0.0**	**2**	**2.69**	**0.7**	**6**	**6.09**	**1.0**	**9**	**12.97**	**0.7**
Cervix uteri	0	0.44	0.0	0	1.19	0.0	0	1.06	0.0	1	2.05	0.5	1	4.74	0.2
Corpus uteri	1	0.30	3.3	0	0.78	0.0	1	0.71	1.4	2	1.77	1.1	4	3.55	1.1
Uterus, NOS	0	0.03	0.0	0	0.06	0.0	0	0.05	0.0	0	0.09	0.0	0	0.23	0.0
Ovary, fallopian tubes	0	0.32	0.0	0	0.84	0.0	1	0.74	1.4	1	1.83	0.5	2	3.73	0.5
Prostate gland	0	0.98	0.0	3	2.13	1.4	1	1.55	0.6	3	3.18	0.9	7	7.82	0.9
Testis	0	0.05	0.0	0	0.13	0.0	0	0.11	0.0	1	0.20	5.1	1	0.49	2.0
Kidney, renal pelvis, ureter	3	0.37	8.1^b	0	0.86	0.0	1	0.69	1.4	1	1.69	0.6	5	3.62	1.4
Bladder, other urinary	0	0.70	0.0	3	1.61	1.9	0	1.27	0.0	1	3.10	0.3	4	6.67	0.6
Melanoma of the skin	0	0.14	0.0	1	0.36	2.8	0	0.30	0.0	2	0.78	2.6	3	1.59	1.9
Eye	0	0.04	0.0	0	0.10	0.0	1	0.08	12.5	0	0.16	0.0	1	0.38	2.6
Brain, central nervous system	0	0.25	0.0	0	0.62	0.0	1	0.52	1.9	2	1.17	1.7	3	2.57	1.2
Thyroid gland	0	0.06	0.0	0	0.14	0.0	0	0.12	0.0	0	0.29	0.0	0	0.60	0.0
Bone	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.10	0.0	0	0.24	0.0
Connective tissue	0	0.06	0.0	0	0.12	0.0	0	0.09	0.0	0	0.17	0.0	0	0.45	0.0
Lymphatic, hematopoietic system	**0**	**0.78**	**0.0**	**2**	**1.80**	**1.1**	**3**	**1.44**	**2.1**	**6**	**3.36**	**1.8**	**11**	**7.37**	**1.5**
Non-Hodgkin's lymphoma	0	0.21	0.0	1	0.48	2.1	1	0.39	2.6	4	0.96	4.2^b	6	2.04	2.9^b
Hodgkin's disease	0	0.07	0.0	0	0.17	0.0	0	0.14	0.0	1	0.28	3.6	1	0.65	1.5
Multiple myeloma	0	0.14	0.0	0	0.32	0.0	1	0.25	4.0	1	0.64	1.6	2	1.36	1.5
Leukemias	0	0.36	0.0	1	0.81	1.2	1	0.63	1.6	0	1.44	0.0	2	3.24	0.6
Chronic lymphocytic	0	0.18	0.0	0	0.40	0.0	1	0.30	3.3	0	0.68	0.0	1	1.56	0.6
Acute nonlymphocytic	0	0.08	0.0	0	0.20	0.0	0	0.17	0.0	0	0.45	0.0	0	0.90	0.0

[a] ICD-7 code = 197.

[b] $P < .05$.

CONNECTIVE
MALES

TABLE 6D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the connective tissue among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,224			852			436			286			1,224		
Person-yr in interval	1,031			2,318			1,736			2,955			8,040		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**5**	**7.57**	**0.7**	**13**	**16.58**	**0.8**	**11**	**12.15**	**0.9**	**31**	**25.02**	**1.2**	**60**	**61.31**	**1.0**
All excluding site of initial cancer	**5**	**7.53**	**0.7**	**13**	**16.51**	**0.8**	**11**	**12.10**	**0.9**	**31**	**24.94**	**1.2**	**60**	**61.07**	**1.0**
Buccal cavity, pharynx	**0**	**0.26**	**0.0**	**0**	**0.57**	**0.0**	**1**	**0.41**	**2.4**	**0**	**0.79**	**0.0**	**1**	**2.04**	**0.5**
Lip	0	0.15	0.0	0	0.32	0.0	1	0.23	4.4	0	0.42	0.0	1	1.11	0.9
Tongue	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.06	0.0	0	0.15	0.0
Salivary gland	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.07	0.0	0	0.17	0.0
Gum, other mouth	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	0	0.12	0.0	0	0.28	0.0
Pharynx	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.13	0.0	0	0.32	0.0
Digestive system	**3**	**3.03**	**1.0**	**3**	**6.43**	**0.5**	**1**	**4.51**	**0.2**	**12**	**8.37**	**1.4**	**19**	**22.35**	**0.9**
Esophagus	0	0.14	0.0	0	0.30	0.0	0	0.20	0.0	0	0.35	0.0	0	1.00	0.0
Stomach	3	1.04	2.9	1	2.15	0.5	0	1.44	0.0	2	2.26	0.9	6	6.89	0.9
Colon	0	0.65	0.0	1	1.41	0.7	0	1.02	0.0	3	2.07	1.4	4	5.15	0.8
Rectum	0	0.67	0.0	0	1.43	0.0	0	1.01	0.0	4	1.89	2.1	4	5.00	0.8
Liver, biliary	0	0.14	0.0	0	0.32	0.0	0	0.24	0.0	2	0.54	3.7	2	1.23	1.6
Pancreas	0	0.27	0.0	0	0.61	0.0	1	0.46	2.2	1	1.01	1.0	2	2.35	0.9
Respiratory system	**2**	**1.38**	**1.5**	**3**	**3.16**	**0.9**	**3**	**2.45**	**1.2**	**8**	**5.81**	**1.4**	**16**	**12.80**	**1.3**
Nasal cavities, sinuses	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.07	0.0	0	0.18	0.0
Larynx	0	0.10	0.0	0	0.23	0.0	0	0.17	0.0	1	0.41	2.5	1	0.91	1.1
Trachea, bronchus, lung	2	1.19	1.7	3	2.74	1.1	3	2.13	1.4	7	5.11	1.4	15	11.17	1.3
Prostate gland	0	0.98	0.0	3	2.13	1.4	1	1.55	0.6	3	3.18	0.9	7	7.82	0.9
Testis	0	0.05	0.0	0	0.13	0.0	0	0.11	0.0	1	0.20	5.1	1	0.49	2.0
Kidney, renal pelvis, ureter	0	0.24	0.0	0	0.53	0.0	1	0.40	2.5	1	0.87	1.1	2	2.04	1.0
Bladder, other urinary	0	0.56	0.0	2	1.27	1.6	0	0.97	0.0	1	2.23	0.4	3	5.03	0.6
Melanoma of the skin	0	0.07	0.0	1	0.16	6.4	0	0.12	0.0	1	0.28	3.6	2	0.63	3.2
Eye	0	0.02	0.0	0	0.06	0.0	1	0.04	25.2	0	0.08	0.0	1	0.20	5.0
Brain, central nervous system	0	0.14	0.0	0	0.32	0.0	1	0.25	4.0	0	0.51	0.0	1	1.22	0.8
Thyroid gland	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.08	0.0	0	0.18	0.0
Bone	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.05	0.0	0	0.13	0.0
Connective tissue	0	0.04	0.0	0	0.07	0.0	0	0.05	0.0	0	0.08	0.0	0	0.24	0.0
Lymphatic, hematopoietic system	**0**	**0.50**	**0.0**	**1**	**1.10**	**0.9**	**1**	**0.83**	**1.2**	**3**	**1.71**	**1.8**	**5**	**4.14**	**1.2**
Non-Hodgkin's lymphoma	0	0.13	0.0	0	0.28	0.0	0	0.22	0.0	2	0.46	4.3	2	1.09	1.8
Hodgkin's disease	0	0.04	0.0	0	0.10	0.0	0	0.08	0.0	1	0.15	6.7	1	0.37	2.7
Multiple myeloma	0	0.09	0.0	0	0.19	0.0	0	0.14	0.0	0	0.31	0.0	0	0.73	0.0
Leukemias	0	0.24	0.0	1	0.52	1.9	1	0.38	2.6	0	0.77	0.0	2	1.90	1.1
Chronic lymphocytic	0	0.13	0.0	0	0.28	0.0	1	0.20	4.9	0	0.40	0.0	1	1.01	1.0
Acute nonlymphocytic	0	0.05	0.0	0	0.12	0.0	0	0.09	0.0	0	0.22	0.0	0	0.47	0.0

[a] ICD-7 code = 197.

[b] $P < .05$.

CONNECTIVE
FEMALES

TABLE 6E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial cancer of the connective tissue among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,094			812			498			333			1,094		
Person-yr in interval	943			2,437			2,035			3,910			9,325		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**5.64**	**0.7**	**10**	**13.77**	**0.7**	**13**	**11.89**	**1.1**	**36**	**29.86**	**1.2**	**63**	**61.16**	**1.0**
All excluding site of initial cancer	**4**	**5.62**	**0.7**	**10**	**13.72**	**0.7**	**13**	**11.85**	**1.1**	**36**	**29.77**	**1.2**	**63**	**60.95**	**1.0**
Buccal cavity, pharynx	**0**	**0.08**	**0.0**	**0**	**0.18**	**0.0**	**0**	**0.15**	**0.0**	**1**	**0.38**	**2.6**	**1**	**0.79**	**1.3**
Lip	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	1	0.06	16.9	1	0.12	8.5
Tongue	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.06	0.0	0	0.13	0.0
Salivary gland	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.08	0.0	0	0.19	0.0
Gum, other mouth	0	0.02	0.0	0	0.04	0.0	0	0.04	0.0	0	0.12	0.0	0	0.22	0.0
Pharynx	0	0.01	0.0	0	0.03	0.0	0	0.03	0.0	0	0.07	0.0	0	0.14	0.0
Digestive system	**0**	**1.91**	**0.0**	**1**	**4.34**	**0.2**	**2**	**3.65**	**0.5**	**10**	**9.25**	**1.1**	**13**	**19.15**	**0.7**
Esophagus	0	0.06	0.0	0	0.12	0.0	0	0.10	0.0	0	0.24	0.0	0	0.51	0.0
Stomach	0	0.55	0.0	1	1.15	0.9	1	0.92	1.1	1	1.85	0.5	3	4.47	0.7
Colon	0	0.56	0.0	0	1.32	0.0	1	1.14	0.9	6	3.17	1.9	7	6.19	1.1
Rectum	0	0.34	0.0	0	0.79	0.0	0	0.67	0.0	1	1.69	0.6	1	3.49	0.3
Liver, biliary	0	0.15	0.0	0	0.35	0.0	0	0.30	0.0	0	0.90	0.0	0	1.70	0.0
Pancreas	0	0.17	0.0	0	0.41	0.0	0	0.36	0.0	1	1.08	0.9	1	2.03	0.5
Respiratory system	**0**	**0.25**	**0.0**	**4**	**0.64**	**6.2**^{b}	**0**	**0.56**	**0.0**	**2**	**1.75**	**1.1**	**6**	**3.20**	**1.9**
Nasal cavities, sinuses	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.04	0.0	0	0.09	0.0
Larynx	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.07	0.0	0	0.14	0.0
Trachea, bronchus, lung	0	0.21	0.0	3	0.54	5.6^{b}	0	0.47	0.0	1	1.52	0.7	4	2.74	1.5
Female breast	0	1.19	0.0	2	3.01	0.7	7	2.60	2.7^{b}	11	6.52	1.7	20	13.33	1.5
Female genital tract	**1**	**1.16**	**0.9**	**0**	**3.04**	**0.0**	**2**	**2.69**	**0.7**	**6**	**6.09**	**1.0**	**9**	**12.97**	**0.7**
Cervix uteri	0	0.44	0.0	0	1.19	0.0	0	1.06	0.0	1	2.05	0.5	1	4.74	0.2
Corpus uteri	1	0.30	3.3	0	0.78	0.0	1	0.71	1.4	2	1.77	1.1	4	3.55	1.1
Uterus, NOS	0	0.03	0.0	0	0.06	0.0	0	0.05	0.0	0	0.09	0.0	0	0.23	0.0
Ovary, fallopian tubes	0	0.32	0.0	0	0.84	0.0	1	0.74	1.4	1	1.83	0.5	2	3.73	0.5
Kidney, renal pelvis, ureter	3	0.13	22.4^{b}	0	0.33	0.0	0	0.29	0.0	0	0.82	0.0	3	1.58	1.9
Bladder, other urinary	0	0.14	0.0	1	0.34	3.0	0	0.30	0.0	0	0.87	0.0	1	1.64	0.6
Melanoma of the skin	0	0.07	0.0	0	0.20	0.0	0	0.18	0.0	1	0.50	2.0	1	0.96	1.0
Eye	0	0.02	0.0	0	0.04	0.0	0	0.04	0.0	0	0.08	0.0	0	0.18	0.0
Brain, central nervous system	0	0.11	0.0	0	0.30	0.0	0	0.27	0.0	2	0.66	3.0	2	1.35	1.5
Thyroid gland	0	0.04	0.0	0	0.09	0.0	0	0.08	0.0	0	0.21	0.0	0	0.42	0.0
Bone	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.05	0.0	0	0.11	0.0
Connective tissue	0	0.02	0.0	0	0.05	0.0	0	0.04	0.0	0	0.09	0.0	0	0.21	0.0
Lymphatic, hematopoietic system	**0**	**0.28**	**0.0**	**1**	**0.70**	**1.4**	**2**	**0.61**	**3.3**	**3**	**1.65**	**1.8**	**6**	**3.23**	**1.9**
Non-Hodgkin's lymphoma	0	0.08	0.0	1	0.20	5.1	1	0.17	5.8	2	0.50	4.0	4	0.95	4.2^{b}
Hodgkin's disease	0	0.03	0.0	0	0.07	0.0	0	0.06	0.0	0	0.13	0.0	0	0.28	0.0
Multiple myeloma	0	0.05	0.0	0	0.13	0.0	1	0.11	8.8	1	0.33	3.0	2	0.63	3.2
Leukemias	0	0.12	0.0	0	0.29	0.0	0	0.25	0.0	0	0.67	0.0	0	1.34	0.0
Chronic lymphocytic	0	0.05	0.0	0	0.12	0.0	0	0.10	0.0	0	0.28	0.0	0	0.55	0.0
Acute nonlymphocytic	0	0.03	0.0	0	0.08	0.0	0	0.08	0.0	0	0.23	0.0	0	0.43	0.0

[a] ICD-7 code = 197.

[b] $P < .05$.

Second Cancer Following Lymphatic and Hematopoietic Cancers in Denmark, 1943–80 [1]

Hans H. Storm *and* Anne Prener [2, 3]

ABSTRACT—In Denmark, approximately 5% of all malignant neoplasms occur within the lymphatic and hematopoietic tissues. Between 1943 and 1980, 23,367 persons with these diseases fulfilled the criteria for entering the study. The risk of developing a second primary cancer was significantly increased only after Hodgkin's disease [relative risk (RR) = 1.6], whereas no increase was found after non-Hodgkin's lymphoma [(NHL); RR = 1.0] or leukemia (RR = 1.1), and a significant deficit occurred after multiple myeloma (RR = 0.8). All initial cancer sites showed a higher incidence of second primary cancers among males than females. Significant elevated risks for acute nonlymphocytic leukemia occurred after Hodgkin's disease (RR = 17), NHL (3.8), and multiple myeloma (9.1). Among persons initially diagnosed with leukemia, NHL was significantly elevated (RR = 2.6). However, these RR should be regarded as minimum figures due to the likelihood of serious underreporting of second primary hematologic cancers in Denmark. The secondary leukemias were likely induced by the treatment of the first primary cancer (chemotherapy, radiotherapy), but common etiologies, misclassification, or progression of the initial cancer cannot be ruled out entirely. Other second primary cancers found to be above expectation following Hodgkin's disease were cancers of the pancreas, lung, and urinary bladder. The risk for bladder cancer increased with time, which suggested a causal relation to radiation or chemotherapy, or both. Cancers of the colon and rectum following NHL and female breast cancer following leukemia occurred below expectation and remain unexplained.—Natl Cancer Inst Monogr 68: 389–410, 1985.

HODGKIN'S DISEASE (ICD-7, 201)

Hodgkin's disease is relatively uncommon, constituting only 0.7% of all cancers in Denmark in 1980 (*1*). The age-standardized incidence rates for 1978–80 were 2.7 and 1.7/100,000 among men and women, respectively (*1*). Incidence rates increased since 1943 to 3.3 for men and 2.1 for women in 1972 and then decreased slightly (*2*). At almost all ages, men have a higher incidence of Hodgkin's disease than do women.

The 5-year relative survival rate as reported from the Norwegian Cancer Registry is 56% for men and 47% for women, all ages and stages combined (*3*). The prognosis has improved during the last 15 years, and the nationwide Danish study on Hodgkin's disease reports survival after 8 years at 69% and more than 90% for low stage disease (*4*).

Hodgkin's disease is related to socioeconomic status with the greatest risk found for those in higher social classes. Other possible risk factors for Hodgkin's disease include occupational exposures (woodworking and chemicals), viruses (Epstein-Barr virus infection and tonsillitis), and immunodeficiency states (*5*). Previous studies of patients treated for Hodgkin's disease have revealed an excess of second cancers (*6*), primarily ANLL (*7–9*) and NHL (*10*). The development of these second cancers is thought to be related to treatment with alkylating agents alone or in combination with radiation.

Results

The Registry received notification between 1943 and 1980 of 3,849 persons with Hodgkin's disease who fulfilled the criteria for entering the study, i.e., they lived 2 or more months after initial diagnosis without developing a second cancer. The average age at diagnosis was 42 years for men and women. The average follow-up was 5 years for women and 4.3 years for men. Radiotherapy alone or as part of the initial treatment was received by 65% of patients.

Overall, 105 patients reported to the Registry developed a second primary cancer following the initial diagnosis of Hodgkin's disease, whereas only 64 were expected based on the general population incidence rates (RR = 1.64; 95% CI = 1.34–1.98). The increased RR was present for women (1.5) and men (1.7). The risk for second cancer development increased with time since diagnosis ($P < .001$ for trend). The reliability of the second cancer diagnosis was high, inasmuch as 93% of the second primary cancers were histologically verified.

Significant excesses for second cancers of the pancreas (RR = 2.8), lung (RR = 2.5), and bladder (RR = 3.8), and ANLL (RR = 17) were observed. The risk for bladder cancer increased over time ($P < .001$ for trend). Some differences in second cancer development by sex were present. The significant excess for bladder cancer was due to an excess among women, and ANLL was more frequent among men. Although based on only 4 cases, the risk in females for developing lung cancer increased until 10 years after the diagnosis of Hodgkin's disease. This contrasts with the picture in males, which shows an ele-

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ABBREVIATIONS: ICD-7 = International Classification of Diseases, Seventh Revision; ANLL = acute nonlymphocytic leukemia; NHL = non-Hodgkin's lymphoma(s); RR = relative risk(s); CI = confidence intervals; CLL = chronic lymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Hans H. Storm, M.D.

[3] We thank Dr. Jens Pedersen-Bjergaard, Department of Medicine, Finsen Institute, Copenhagen, Denmark for his valuable suggestions during the preparation of this manuscript.

vated risk throughout all intervals. For women followed for 10 or more years, a significant excess risk was seen for bone cancer and brain tumors. No cancer of any site occurred significantly below expectation.

Discussion

Hodgkin's disease has been intensely studied so that survival and cure rates could be improved. In Denmark, a national clinical trial with uniform staging and centralized randomization to various treatments was performed in 1971–79 (*4*). With the Registry linked to this trial, reporting of Hodgkin's disease after 1971 is virtually complete. The elevated risk for ANLL demonstrated in this study was not unexpected and had been previously reported (*4, 6, 7, 10*). However, it was surprising that only 10 cases of ANLL were observed in our Registry study, compared with a total of 17 comparable diagnoses reported in other Danish publications (*4, 7, 8*). This finding suggests that underreporting of second hematologic tumors may be a serious problem in cancer registry studies, and the observed excesses must be considered minimum estimates of risk.

Although cigarette smoking and low social class are related to cancers of the lung and bladder, these factors have not been linked to Hodgkin's disease. The increasing risk of bladder cancer over time suggests an effect of antineoplastic drugs or radiation, or both, which 65% of the patients with Hodgkin's disease received. The excess lung cancers might be partially related to high-dose radiotherapy given to the mediastinum and upper abdominal lymph nodes. It is noteworthy that a high risk for cancers of the bladder and lung persisted 10 years or more after initial diagnosis. The risk for ANLL was highest 5–9 years after diagnosis and then decreased slightly, which is compatible with the pattern seen for treatment-induced leukemias by alkylating agents (*7, 8*). It is possible for significant excesses to occur by chance alone, but effects appearing after many years of observation suggest iatrogenic effects. Studies of second primary cancers among Hodgkin's patients provide us with special opportunities to assess the carcinogenic and leukemogenic effects of chemotherapy and radiotherapy, alone or in combination.

NON-HODGKIN'S LYMPHOMA (ICD-7, 200, 202)

Various cancers are included in the NHL that are grouped within the ICD-7 classification used by this Registry. In Denmark, NHL comprise lymphosarcomas, reticulosarcomas, and other specified and unspecified lymphomas (*1*), and represent 1.3% of all malignant neoplasms in Denmark. Survival is poor compared with that of Hodgkin's disease, with a 5-year relative survival rate of 34% for men and 38% for women (*3*). It is more frequent among men, and the male-to-female ratio is 1.6. Urban-rural differences are seen in incidence rates, especially among males (1.8 times higher in urban areas); otherwise, no major differences are known within the Danish population (*2*).

As for Hodgkin's disease and leukemia, various risk factors for NHL have been suggested (*11*): higher socioeconomic class, familial occurrence, genetic or acquired immune deficiency (*5*), radiation (*12, 13*), immunosuppressive drugs (*10*), occupation and exposure to certain herbicides (*14*), infectious agents including the Epstein-Barr virus (*15*), and diet (overnutrition), possibly linked to socioeconomic status (*16*). Most investigators have not distinguished between the subtypes of NHL in studies of possible risk factors.

Results

Included in this analysis are 3,655 men and 2,886 women whose diagnoses of NHL were reported to the Registry from 1943 to 1980. The average age at diagnosis was 58 years, 57 for men and 60 for women. The average follow-up was 3.5 years, and a total of 22,905 person-years was accumulated. Radiotherapy was received by 63% of patients as part of their initial treatment. However, radiotherapy was not always administered alone because 40% of patients were coded as also receiving "other nonsurgical treatment," which included chemotherapy.

Overall, 207 (or 3.2%) of the patients with NHL developed a second primary cancer. Confirmation of 85% of the second primary cancers was based on histology, and 83% of the corresponding NHL were histologically confirmed. No overall excess of second cancers was found, 207 were observed and 204 expected (RR = 1.01; 95% CI = 0.88–1.16). However, for both sexes combined, a significant excess was seen for ANLL (RR = 3.8; 95% CI = 1.4–8.3) that was confined mainly to men. The risk increased over time since diagnosis, though not significantly, and was present 10 or more years after initial diagnosis. A nonsignificant excess was observed in all intervals for melanoma (RR = 1.7) and cancer of the liver and gallbladder (RR = 1.7). Overall deficits were observed for second primary cancers of the colon (RR = 0.7; 95% CI = 0.4–1.2) and rectum (RR = 0.3; 95% CI = 0.1–0.7).

Discussion

The observed excesses of ANLL have been described previously (*17*) and were attributed to the use of alkylating agents or radiation therapy, although misinterpretation of the leukemic phase that appears in more than 7% of the patients with NHL could have also contributed to reported excesses (*18*). A recent Danish study (*19*) reported 5 cases of ANLL following NHL within only 10 years of observation, with all cases confirmed by cytologic studies. In contrast, only 6 cases of ANLL were reported to the Danish Cancer Registry during 40 years of operation. Even if changes in diagnostic specificity have occurred with time, it is obvious that for NHL, as for Hodgkin's disease, there has been serious underreporting of second primary hematologic cancers. Therefore, the excess RR of ANLL must be considered as a minimum risk estimate. The excess of melanoma is consistent with previous reports, and immunologic factors might be responsible for this finding (*5*). The observed deficit of colon cancer was not expected in light of the fact that colon cancer, like NHL, is most common in the upper social classes. Further studies are needed for investigation and clarification of the risk factors for the various subtypes of NHL.

MULTIPLE MYELOMA (ICD-7, 203)

Multiple myeloma constitutes 0.3% of all malignant neoplasms in Denmark (*1*). The disease, characterized by abnormal protein metabolism (*20*), is seldom diagnosed below the age of 50 years (*21*). The age-standardized incidence rate for 1980 was 2.0/100,000 for men and 1.8/100,000 for women. The male-to-female ratio is 1.4 and has been stable ever since 1943 (*2*). No substantial urban-rural differences in risk exist (*2*). The 5-year relative survival rate is 18% for both men and women (*3*).

The diagnosis of multiple myeloma in the 1940s and 1950s was largely based on x rays. In more recent years, the diagnosis was based on protein electrophoresis and bone marrow biopsies showing more than 15% abnormal and multinucleated plasma cells. Studies of chromosomes may further ensure the diagnosis in the future (*22, 23*). As with leukemia, few risk factors have been identified, although radiation, familial predisposition, and some chemical exposures have been suggested. Based on an unpublished linkage study performed by the Registry, it appears that the underreporting of multiple myeloma, as demonstrated in Norway (*24*), also occurs in Denmark.

Results

Between 1943 and 1980, multiple myeloma occurred in 1,867 males and 1,615 females who were included in the study. The average age at diagnosis was 66 years. Approximately 28% of the patients received radiation as part of their initial treatment. Most second primary cancers were histologically verified (82%), constituting a fair basis for studies on second primary cancers; 12% of the corresponding myeloma diagnoses were made by means other than microscopy. The observed number of second primary cancers for both sexes was 68 versus 88 expected, a deficit which was statistically significant (RR = 0.8; 95% CI = 0.60–0.98). For both sexes combined and for males alone, an increased risk for ANLL was found, although the excess was based on only 6 observed cases and was seen only in the first 5 years after diagnosis of multiple myeloma. Two observed cases of NHL versus 0.12 expected occurred 10 or more years after myeloma diagnosis. An overall significant excess of kidney cancer (RR = 2.9; 95% CI = 1.3–5.8) was due solely to cancer development within the first year of follow-up.

Discussion

Few Danish studies indicating risks of second primary cancers following multiple myeloma have been published. However, the finding of 6 cases of acute leukemias in a small hospital-based series within a few years of observation (*25*) versus a total of 6 of ANLL reported to the Registry during a 37-year period indicates that reporting or acceptance of a second primary hematologic cancer is as poor following the diagnosis of multiple myeloma as it is for Hodgkin's disease and NHL.

Rosner and Grünwald (*26*) described ANLL among long-term survivors with multiple myeloma. The therapeutic use of radiation might be causally related to this excess (*27*), but it is more likely that therapy with an alkylating agent is the predominant factor (*28*). The excess of NHL might be accidental, but it is plausible that this tumor type would follow multiple myeloma, although the possible effect of radiotherapy in causing NHL is not convincing (*29*). The excess of kidney cancer could be due to common risk factors, but the effect of close medical surveillance probably influenced these findings. Detailed studies of leukemia and lymphoma as second primary cancers after multiple myeloma might provide useful information on the mechanisms of cancer causation following exposure to antineoplastic drugs and radiation.

LEUKEMIA (ICD-7, 204)

Leukemias account for 2.6% of all cancer in Denmark with the incidence in males 1.5 times that in females; CLL accounts for 38% of all leukemias (*2, 30*). An evaluation of all leukemias together is crude because CLL differs considerably from the other types. For example, CLL is characterized by the absence of specific chromosome changes, few terminal blast crises, and fairly good survival, relative to other types of leukemia [the 5-yr relative survival rate is 34%; (*3*)]. It occurs predominantly among the elderly, contrary to acute lymphocytic leukemia which predominantly affects younger people. The myelogenous leukemias have an age structure in between CLL and acute lymphocytic leukemia. Survival is poor for acute lymphocytic and myelogenous leukemias; the 5-yr relative survival rate ranges from 7% to 13% (*3*).

Little is known about the etiology of leukemia. Based on the results of animal experiments and recent human studies of T-cell leukemia (*31*), some physicians think that viruses have an etiologic role. Family history, radiation, immune deficiency, and exposure to certain chemicals (especially benzene) and antineoplastic drugs have also been identified as risk factors (*32*).

Treatment of leukemias includes the use of radiation and antineoplastic drugs that themselves can be causally related to cancer induction. Various drugs have been used to treat the acute and myelogenous leukemias. For many patients with CLL, only small doses of a single agent, chlorambucil, have been administered.

Results

Of 9,495 persons with leukemia who lived 2 or more months, 218 experienced a second tumor: 152 men and 66 women. Average age (54 yr) and year of primary leukemia diagnosis (1965) was the same for both sexes. The average follow-up time was 2.2 years, and only 21,168 person-years were available for risk calculations.

Most (77%) persons with leukemia who developed a second primary cancer had histologic confirmation of both the leukemia and the second primary tumor. A relatively high proportion (13%) of second cancers, perhaps reflecting the older ages of the patients with CLL, was verified only by clinical means or autopsy. The proportion of second cancers verified only by death certificates was approximately 4%.

A marginally significant observed-to-expected ratio of 1.2 for all second cancers among men was seen (95% CI = 1.0–1.4). However, for all sites and both sexes combined, 218 second cancers were observed versus 205 expected (RR = 1.06; 95% CI = 0.93–1.21). The most striking findings seen in both sexes were the increased risk of NHL (RR = 2.6; 95% CI = 1.2–5.0) and cancer of the kidney (RR = 2.9; 95% CI = 1.7–4.5). Based on 7 observed cases and 2.3 expected, we noted that cancer of the lip also occurred above expectation. Among women, a significant deficit for second breast cancers was observed (RR = 0.4; 95% CI = 0.2–0.9).

Discussion

Whereas the risk of leukemia as a second cancer has been extensively studied (*7, 19, 33, 34*), the risk of cancer following leukemia has received little attention, with the possible exception of CLL (*35*). That few studies of multiple primary cancer among leukemia patients have been conducted is probably due to the extremely poor survival (until recently) following this uncommon disease, and the low probability of the patient living long enough for a new cancer to develop. The findings in our study are thus largely attributable to cancers following CLL because it is characterized by relatively good survival and large numbers compared with the other leukemias. In our study, excesses of NHL and cancers of the kidney and lip were noted; breast cancer was infrequent among persons first diagnosed with leukemia. Whether the excess of NHL is real or an artifact is difficult for us to establish, inasmuch as leukemias as part of their natural history are known to terminate into lymphomas or lymph node involvement. However, the observed number of NHL is probably an underestimate; the Danish Cancer Registry and the notifying clinicians are hesitant to accept new hematologic cancers as valid diagnoses. The excess of kidney cancer can partly be explained by the closer surveillance and slightly higher autopsy rates among cancer patients, but the increasing trend with time indicates that further studies of this association are needed. A previously suggested association between CLL and melanoma and connective tissue tumors (*35*) is partially supported by the observation of nonsignificant increased risks. Lung cancer, on the other hand, was not found in excess (*35*). Because of the large number of multiple comparisons made, chance might be the reason for the unexpected low risk of breast cancer following leukemia. One could speculate, though, that the use of antineoplastic drugs in conjunction with treatment for the leukemias could be responsible for the suppression of some preclinical breast cancers.

NOTE ADDED IN PROOF

After the completion of this study and discussion of its results, the Danish Cancer Registry received notification of 17 cases of ANLL, 13 following Hodgkin's disease, 3 following NHL, and 1 following multiple myeloma. All these cases were diagnosed during the period from 1976 to 1980.

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NH LYMPHOMA
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial non-Hodgkin's lymphoma, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	3,655	2,886	6,541
No. who developed a second primary cancer	105	102	207
Average age at diagnosis of first cancer, yr	57	60	58
Average yr of diagnosis of first cancer	1966	1967	1966
Person-yr of follow-up	12,462	10,443	22,905
Average follow-up, yr	3.4	3.6	3.5
Percent given radiotherapy for first cancer	63	63	63

[a] ICD-7 codes = 200, 202.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after an initial non-Hodgkin's lymphoma in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	151	73.0
Only the first cancer	21	10.2
Only the second cancer	25	12.1
Neither first nor second cancer	10	4.8
Total second primary cancers	207	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

NH LYMPHOMA
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial non-Hodgkin's lymphoma among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	6,541			3,418			1,331			699			6,541		
Person-yr in interval	4,729			8,094			4,834			5,247			22,905		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**33**	**41.20**	**0.8**	**62**	**68.94**	**0.9**	**49**	**42.94**	**1.1**	**63**	**50.91**	**1.2**	**207**	**203.98**	**1.0**
All excluding site of initial cancer	**33**	**40.50**	**0.8**	**58**	**67.76**	**0.9**	**48**	**42.20**	**1.1**	**59**	**50.01**	**1.2**	**198**	**200.45**	**1.0**
Buccal cavity, pharynx	**0**	**1.01**	**0.0**	**3**	**1.64**	**1.8**	**4**	**0.99**	**4.0**[b]	**1**	**1.16**	**0.9**	**8**	**4.79**	**1.7**
Lip	0	0.46	0.0	1	0.73	1.4	3	0.43	7.0[b]	0	0.50	0.0	4	2.11	1.9
Tongue	0	0.10	0.0	1	0.16	6.3	0	0.09	0.0	0	0.11	0.0	1	0.47	2.1
Salivary gland	0	0.11	0.0	0	0.18	0.0	0	0.11	0.0	0	0.12	0.0	0	0.53	0.0
Gum, other mouth	0	0.18	0.0	0	0.29	0.0	1	0.18	5.6	0	0.23	0.0	1	0.89	1.1
Pharynx	0	0.16	0.0	1	0.27	3.7	0	0.16	0.0	1	0.19	5.3	2	0.79	2.5
Digestive system	**11**	**14.80**	**0.7**	**19**	**23.89**	**0.8**	**11**	**14.88**	**0.7**	**13**	**17.50**	**0.7**	**54**	**71.08**	**0.8**[b]
Esophagus	1	0.56	1.8	0	0.87	0.0	0	0.54	0.0	0	0.62	0.0	1	2.58	0.4
Stomach	4	4.23	0.9	8	6.45	1.2	4	3.87	1.0	4	4.29	0.9	20	18.85	1.1
Colon	3	3.92	0.8	6	6.51	0.9	3	4.17	0.7	2	5.12	0.4	14	19.72	0.7
Rectum	0	3.01	0.0	2	4.88	0.4	1	3.00	0.3	1	3.49	0.3	4	14.39	0.3[b]
Liver, biliary	1	1.01	1.0	2	1.73	1.2	2	1.12	1.8	4	1.39	2.9	9	5.26	1.7
Pancreas	2	1.54	1.3	1	2.61	0.4	1	1.67	0.6	2	2.05	1.0	6	7.88	0.8
Respiratory system	**5**	**5.88**	**0.9**	**4**	**10.19**	**0.4**	**12**	**6.30**	**1.9**	**13**	**7.67**	**1.7**	**34**	**30.03**	**1.1**
Nasal cavities, sinuses	0	0.10	0.0	0	0.16	0.0	0	0.09	0.0	1	0.11	9.1	1	0.45	2.2
Larynx	0	0.38	0.0	1	0.66	1.5	2	0.39	5.1	0	0.49	0.0	3	1.92	1.6
Trachea, bronchus, lung	5	5.12	1.0	3	8.90	0.3[b]	10	5.51	1.8	11	6.72	1.6	29	26.24	1.1
Female breast	4	3.63	1.1	5	6.38	0.8	3	4.00	0.7	9	4.58	2.0	21	18.60	1.1
Female genital tract	**1**	**3.24**	**0.3**	**9**	**5.76**	**1.6**	**5**	**3.53**	**1.4**	**3**	**3.82**	**0.8**	**18**	**16.35**	**1.1**
Cervix uteri	0	1.03	0.0	6	1.85	3.2[b]	2	1.13	1.8	0	1.14	0.0	8	5.14	1.6
Corpus uteri	0	0.94	0.0	0	1.67	0.0	1	1.02	1.0	0	1.13	0.0	1	4.77	0.2
Uterus, NOS	0	0.08	0.0	0	0.12	0.0	0	0.07	0.0	0	0.08	0.0	0	0.35	0.0
Ovary, fallopian tubes	1	0.98	1.0	3	1.74	1.7	1	1.07	0.9	3	1.19	2.5	8	4.98	1.6
Prostate gland	2	3.08	0.6	1	4.94	0.2	2	3.17	0.6	3	4.00	0.7	8	15.19	0.5
Testis	1	0.14	7.3	1	0.24	4.2	1	0.15	6.6	0	0.20	0.0	3	0.72	4.1
Kidney, renal pelvis, ureter	4	1.25	3.2	1	2.12	0.5	2	1.33	1.5	3	1.60	1.9	10	6.30	1.6
Bladder, other urinary	1	2.44	0.4	3	4.16	0.7	2	2.62	0.8	4	3.26	1.2	10	12.49	0.8
Melanoma of the skin	1	0.46	2.2	2	0.81	2.5	0	0.51	0.0	1	0.64	1.6	4	2.42	1.7
Eye	0	0.12	0.0	0	0.20	0.0	1	0.12	8.3	0	0.14	0.0	1	0.59	1.7
Brain, central nervous system	0	0.78	0.0	2	1.35	1.5	0	0.81	0.0	1	0.94	1.1	3	3.87	0.8
Thyroid gland	1	0.19	5.3	1	0.32	3.1	0	0.21	0.0	1	0.24	4.2	3	0.96	3.1
Bone	0	0.08	0.0	0	0.12	0.0	0	0.08	0.0	0	0.08	0.0	0	0.35	0.0
Connective tissue	0	0.15	0.0	0	0.24	0.0	0	0.14	0.0	0	0.15	0.0	0	0.67	0.0
Lymphatic, hematopoietic system	**2**	**2.52**	**0.8**	**9**	**4.24**	**2.1**	**4**	**2.66**	**1.5**	**9**	**3.19**	**2.8**[b]	**24**	**12.62**	**1.9**[b]
Non-Hodgkin's lymphoma	0	0.70	0.0	4	1.18	3.4	1	0.74	1.4	4	0.90	4.4[b]	9	3.53	2.5[b]
Hodgkin's disease	2	0.20	10.0[b]	0	0.33	0.0	0	0.21	0.0	1	0.23	4.3	3	0.97	3.1
Multiple myeloma	0	0.47	0.0	0	0.80	0.0	0	0.50	0.0	0	0.61	0.0	0	2.39	0.0
Leukemias	0	1.13	0.0	5	1.88	2.7	3	1.19	2.5	4	1.42	2.8	12	5.61	2.1[b]
Chronic lymphocytic	0	0.56	0.0	2	0.93	2.2	3	0.60	5.0[b]	1	0.72	1.4	6	2.81	2.1
Acute nonlymphocytic	0	0.30	0.0	3	0.52	5.8[b]	0	0.33	0.0	3	0.42	7.1[b]	6	1.57	3.8[b]

[a] ICD-7 codes = 200, 202.

[b] $P < .05$.

NH LYMPHOMA
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial non-Hodgkin's lymphoma among males in Denmark, 1943-80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	3,655			1,862			711			377			3,655		
Person-yr in interval	2,624			4,354			2,576			2,908			12,462		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**17**	**23.53**	**0.7**	**26**	**38.36**	**0.7**[b]	**25**	**23.64**	**1.1**	**37**	**28.79**	**1.3**	**105**	**114.32**	**0.9**
All excluding site of initial cancer	**17**	**23.12**	**0.7**	**24**	**37.68**	**0.6**[b]	**25**	**23.22**	**1.1**	**33**	**28.27**	**1.2**	**99**	**112.28**	**0.9**
Buccal cavity, pharynx	**0**	**0.77**	**0.0**	**2**	**1.23**	**1.6**	**3**	**0.73**	**4.1**	**1**	**0.86**	**1.2**	**6**	**3.59**	**1.7**
Lip	0	0.42	0.0	1	0.67	1.5	2	0.39	5.1	0	0.45	0.0	3	1.93	1.6
Tongue	0	0.06	0.0	0	0.09	0.0	0	0.05	0.0	0	0.06	0.0	0	0.26	0.0
Salivary gland	0	0.06	0.0	0	0.10	0.0	0	0.06	0.0	0	0.07	0.0	0	0.30	0.0
Gum, other mouth	0	0.11	0.0	0	0.17	0.0	1	0.10	9.6	0	0.13	0.0	1	0.52	1.9
Pharynx	0	0.12	0.0	1	0.20	5.0	0	0.12	0.0	1	0.14	6.9	2	0.58	3.4
Digestive system	**5**	**8.61**	**0.6**	**5**	**13.51**	**0.4**[b]	**2**	**8.23**	**0.2**[b]	**6**	**9.76**	**0.6**	**18**	**40.11**	**0.4**[b]
Esophagus	1	0.38	2.6	0	0.58	0.0	0	0.35	0.0	0	0.40	0.0	1	1.71	0.6
Stomach	2	2.65	0.8	2	3.97	0.5	0	2.33	0.0	1	2.60	0.4	5	11.55	0.4
Colon	1	1.98	0.5	2	3.18	0.6	1	1.99	0.5	1	2.50	0.4	5	9.65	0.5
Rectum	0	1.93	0.0	0	3.04	0.0	0	1.85	0.0	1	2.17	0.5	1	9.00	0.1[b]
Liver, biliary	1	0.48	2.1	1	0.80	1.2	1	0.51	2.0	2	0.64	3.1	5	2.43	2.1
Pancreas	0	0.91	0.0	0	1.51	0.0	0	0.95	0.0	1	1.17	0.9	1	4.55	0.2
Respiratory system	**5**	**4.95**	**1.0**	**4**	**8.51**	**0.5**	**11**	**5.24**	**2.1**[b]	**11**	**6.41**	**1.7**	**31**	**25.10**	**1.2**
Nasal cavities, sinuses	0	0.07	0.0	0	0.11	0.0	0	0.06	0.0	1	0.08	12.9	1	0.32	3.1
Larynx	0	0.34	0.0	1	0.59	1.7	2	0.35	5.7	0	0.44	0.0	3	1.72	1.7
Trachea, bronchus, lung	5	4.33	1.2	3	7.47	0.4	9	4.60	2.0	9	5.63	1.6	26	22.03	1.2
Prostate gland	2	3.08	0.6	1	4.94	0.2	2	3.17	0.6	3	4.00	0.7	8	15.19	0.5
Testis	1	0.14	7.3	1	0.24	4.2	1	0.15	6.6	0	0.20	0.0	3	0.72	4.1
Kidney, renal pelvis, ureter	2	0.78	2.6	0	1.30	0.0	1	0.81	1.2	2	0.99	2.0	5	3.88	1.3
Bladder, other urinary	1	1.94	0.5	3	3.28	0.9	2	2.05	1.0	4	2.58	1.5	10	9.85	1.0
Melanoma of the skin	0	0.22	0.0	0	0.37	0.0	0	0.23	0.0	0	0.31	0.0	0	1.13	0.0
Eye	0	0.07	0.0	0	0.12	0.0	0	0.07	0.0	0	0.08	0.0	0	0.35	0.0
Brain, central nervous system	0	0.44	0.0	1	0.74	1.3	0	0.44	0.0	0	0.53	0.0	1	2.15	0.5
Thyroid gland	0	0.07	0.0	1	0.11	8.8	0	0.07	0.0	0	0.08	0.0	1	0.34	3.0
Bone	0	0.05	0.0	0	0.07	0.0	0	0.05	0.0	0	0.05	0.0	0	0.21	0.0
Connective tissue	0	0.09	0.0	0	0.14	0.0	0	0.08	0.0	0	0.09	0.0	0	0.39	0.0
Lymphatic, hematopoietic system	**1**	**1.57**	**0.6**	**6**	**2.58**	**2.3**	**2**	**1.60**	**1.2**	**8**	**1.94**	**4.1**[b]	**17**	**7.70**	**2.2**[b]
Non-Hodgkin's lymphoma	0	0.41	0.0	2	0.68	2.9	0	0.42	0.0	4	0.52	7.7[b]	6	2.04	2.9[b]
Hodgkin's disease	1	0.13	7.9	0	0.21	0.0	0	0.13	0.0	1	0.15	6.7	2	0.62	3.2
Multiple myeloma	0	0.28	0.0	0	0.47	0.0	0	0.29	0.0	0	0.36	0.0	0	1.41	0.0
Leukemias	0	0.73	0.0	4	1.19	3.4	2	0.74	2.7	3	0.90	3.3	9	3.55	2.5[b]
Chronic lymphocytic	0	0.39	0.0	1	0.63	1.6	2	0.40	5.0	1	0.48	2.1	4	1.90	2.1
Acute nonlymphocytic	0	0.18	0.0	3	0.31	9.8[b]	0	0.19	0.0	2	0.25	8.0	5	0.93	5.4[b]

[a] ICD-7 codes = 200, 202.

[b] $P < .05$.

NH LYMPHOMA FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial non-Hodgkin's lymphoma among females in Denmark, 1943–80*^{a}

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,886			1,556			620			322			2,886		
Person-yr in interval	2,105			3,741			2,258			2,339			10,443		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**16**	**17.67**	**0.9**	**36**	**30.58**	**1.2**	**24**	**19.30**	**1.2**	**26**	**22.12**	**1.2**	**102**	**89.66**	**1.1**
All excluding site of initial cancer	**16**	**17.38**	**0.9**	**34**	**30.08**	**1.1**	**23**	**18.98**	**1.2**	**26**	**21.74**	**1.2**	**99**	**88.17**	**1.1**
Buccal cavity, pharynx	**0**	**0.24**	**0.0**	**1**	**0.41**	**2.5**	**1**	**0.26**	**3.9**	**0**	**0.30**	**0.0**	**2**	**1.20**	**1.7**
Lip	0	0.04	0.0	0	0.06	0.0	1	0.04	25.2	0	0.05	0.0	1	0.18	5.4
Tongue	0	0.04	0.0	1	0.07	14.3	0	0.04	0.0	0	0.05	0.0	1	0.21	4.8
Salivary gland	0	0.05	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.23	0.0
Gum, other mouth	0	0.07	0.0	0	0.12	0.0	0	0.08	0.0	0	0.10	0.0	0	0.37	0.0
Pharynx	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.05	0.0	0	0.21	0.0
Digestive system	**6**	**6.19**	**1.0**	**14**	**10.38**	**1.3**	**9**	**6.65**	**1.4**	**7**	**7.74**	**0.9**	**36**	**30.97**	**1.2**
Esophagus	0	0.18	0.0	0	0.29	0.0	0	0.19	0.0	0	0.22	0.0	0	0.87	0.0
Stomach	2	1.58	1.3	6	2.48	2.4	4	1.54	2.6	3	1.69	1.8	15	7.30	2.1^b
Colon	2	1.94	1.0	4	3.33	1.2	2	2.18	0.9	1	2.62	0.4	9	10.07	0.9
Rectum	0	1.08	0.0	2	1.84	1.1	1	1.15	0.9	0	1.32	0.0	3	5.39	0.6
Liver, biliary	0	0.53	0.0	1	0.93	1.1	1	0.61	1.6	2	0.75	2.7	4	2.83	1.4
Pancreas	2	0.63	3.2	1	1.10	0.9	1	0.72	1.4	1	0.88	1.1	5	3.33	1.5
Respiratory system	**0**	**0.93**	**0.0**	**0**	**1.68**	**0.0**	**1**	**1.06**	**0.9**	**2**	**1.26**	**1.6**	**3**	**4.93**	**0.6**
Nasal cavities, sinuses	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Larynx	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	0	0.05	0.0	0	0.20	0.0
Trachea, bronchus, lung	0	0.79	0.0	0	1.43	0.0	1	0.91	1.1	2	1.09	1.8	3	4.21	0.7
Female breast	4	3.63	1.1	5	6.38	0.8	3	4.00	0.7	9	4.58	2.0	21	18.60	1.1
Female genital tract	**1**	**3.24**	**0.3**	**9**	**5.76**	**1.6**	**5**	**3.53**	**1.4**	**3**	**3.82**	**0.8**	**18**	**16.35**	**1.1**
Cervix uteri	0	1.03	0.0	6	1.85	3.2^b	2	1.13	1.8	0	1.14	0.0	8	5.14	1.6
Corpus uteri	0	0.94	0.0	0	1.67	0.0	1	1.02	1.0	0	1.13	0.0	1	4.77	0.2
Uterus, NOS	0	0.08	0.0	0	0.12	0.0	0	0.07	0.0	0	0.08	0.0	0	0.35	0.0
Ovary, fallopian tubes	1	0.98	1.0	3	1.74	1.7	1	1.07	0.9	3	1.19	2.5	8	4.98	1.6
Kidney, renal pelvis, ureter	2	0.47	4.3	1	0.82	1.2	1	0.52	1.9	1	0.61	1.6	5	2.42	2.1
Bladder, other urinary	0	0.50	0.0	0	0.88	0.0	0	0.57	0.0	0	0.68	0.0	0	2.64	0.0
Melanoma of the skin	1	0.24	4.1	2	0.44	4.5	0	0.28	0.0	1	0.33	3.0	4	1.29	3.1
Eye	0	0.05	0.0	0	0.08	0.0	1	0.05	19.7	0	0.06	0.0	1	0.24	4.2
Brain, central nervous system	0	0.34	0.0	1	0.61	1.6	0	0.37	0.0	1	0.41	2.4	2	1.72	1.2
Thyroid gland	1	0.12	8.2	0	0.21	0.0	0	0.14	0.0	1	0.16	6.4	2	0.62	3.2
Bone	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.14	0.0
Connective tissue	0	0.06	0.0	0	0.10	0.0	0	0.06	0.0	0	0.06	0.0	0	0.28	0.0
Lymphatic, hematopoietic system	**1**	**0.95**	**1.1**	**3**	**1.66**	**1.8**	**2**	**1.06**	**1.9**	**1**	**1.25**	**0.8**	**7**	**4.92**	**1.4**
Non-Hodgkin's lymphoma	0	0.29	0.0	2	0.50	4.0	1	0.32	3.1	0	0.38	0.0	3	1.49	2.0
Hodgkin's disease	1	0.07	14.8	0	0.12	0.0	0	0.08	0.0	0	0.08	0.0	1	0.35	2.9
Multiple myeloma	0	0.19	0.0	0	0.33	0.0	0	0.21	0.0	0	0.25	0.0	0	0.98	0.0
Leukemias	0	0.40	0.0	1	0.69	1.4	1	0.45	2.2	1	0.52	1.9	3	2.06	1.5
Chronic lymphocytic	0	0.17	0.0	1	0.30	3.3	1	0.20	5.1	0	0.24	0.0	2	0.91	2.2
Acute nonlymphocytic	0	0.12	0.0	0	0.21	0.0	0	0.14	0.0	1	0.17	6.0	1	0.64	1.6

[a] ICD-7 codes = 200, 202.

[b] $P < .05$.

HODGKIN'S DISEASE
BOTH SEXES

TABLE 2A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial Hodgkin's disease, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	2,307	1,542	3,849
No. who developed a second primary cancer	64	41	105
Average age at diagnosis of first cancer, yr	42	43	42
Average yr of diagnosis of first cancer	1964	1964	1964
Person-yr of follow-up	9,994	7,685	17,679
Average follow-up, yr	4.3	5.0	4.6
Percent given radiotherapy for first cancer	64	67	65

[a] ICD-7 code = 201.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 2B.—*Microscopic confirmation among persons who developed second primary cancers after an initial Hodgkin's disease in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	88	83.8
Only the first cancer	5	4.8
Only the second cancer	10	9.5
Neither first nor second cancer	2	1.9
Total second primary cancers	105	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

HODGKIN'S DISEASE
BOTH SEXES

TABLE 2C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial Hodgkin's disease among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,849			2,738			1,202			534			3,849		
Person-yr in interval	3,277			7,234			4,127			3,040			17,679		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**10**	**11.67**	**0.9**	**27**	**22.68**	**1.2**	**34**	**14.09**	**2.4**[b]	**34**	**15.33**	**2.2**[b]	**105**	**63.78**	**1.6**[b]
All excluding site of initial cancer	**10**	**11.55**	**0.9**	**27**	**22.42**	**1.2**	**34**	**13.95**	**2.4**[b]	**34**	**15.23**	**2.2**[b]	**105**	**63.16**	**1.7**[b]
Buccal cavity, pharynx	**0**	**0.32**	**0.0**	**0**	**0.60**	**0.0**	**1**	**0.37**	**2.7**	**1**	**0.37**	**2.7**	**2**	**1.65**	**1.2**
Lip	0	0.15	0.0	0	0.28	0.0	0	0.16	0.0	0	0.17	0.0	0	0.76	0.0
Tongue	0	0.03	0.0	0	0.05	0.0	1	0.03	33.3	0	0.03	0.0	1	0.14	7.1
Salivary gland	0	0.04	0.0	0	0.09	0.0	0	0.05	0.0	0	0.04	0.0	0	0.21	0.0
Gum, other mouth	0	0.04	0.0	0	0.09	0.0	0	0.06	0.0	0	0.06	0.0	0	0.25	0.0
Pharynx	0	0.05	0.0	0	0.10	0.0	0	0.06	0.0	1	0.07	14.3	1	0.30	3.3
Digestive system	**2**	**3.72**	**0.5**	**10**	**6.62**	**1.5**	**5**	**3.94**	**1.3**	**5**	**4.23**	**1.2**	**22**	**18.50**	**1.2**
Esophagus	0	0.14	0.0	0	0.24	0.0	0	0.15	0.0	1	0.15	6.7	1	0.67	1.5
Stomach	0	1.05	0.0	3	1.71	1.8	2	0.96	2.1	0	0.94	0.0	5	4.66	1.1
Colon	1	0.96	1.0	3	1.79	1.7	0	1.12	0.0	0	1.24	0.0	4	5.11	0.8
Rectum	0	0.79	0.0	1	1.42	0.7	1	0.84	1.2	2	0.91	2.2	4	3.95	1.0
Liver, biliary	0	0.25	0.0	2	0.46	4.3	0	0.28	0.0	0	0.32	0.0	2	1.31	1.5
Pancreas	1	0.40	2.5	1	0.74	1.4	2	0.45	4.4	2	0.52	3.8	6	2.11	2.8[b]
Respiratory system	**4**	**1.72**	**2.3**	**6**	**3.39**	**1.8**	**8**	**2.09**	**3.8**[b]	**5**	**2.49**	**2.0**	**23**	**9.68**	**2.4**[b]
Nasal cavities, sinuses	0	0.03	0.0	1	0.05	20.0	0	0.04	0.0	0	0.04	0.0	1	0.15	6.7
Larynx	0	0.12	0.0	0	0.24	0.0	1	0.16	6.3	0	0.17	0.0	1	0.69	1.4
Trachea, bronchus, lung	4	1.48	2.7	5	2.95	1.7	7	1.81	3.9[b]	5	2.18	2.3	21	8.42	2.5[b]
Female breast	2	1.06	1.9	0	2.24	0.0	0	1.53	0.0	4	1.69	2.4	6	6.51	0.9
Female genital tract	**0**	**1.15**	**0.0**	**0**	**2.46**	**0.0**	**2**	**1.60**	**1.3**	**1**	**1.63**	**0.6**	**3**	**6.84**	**0.4**
Cervix uteri	0	0.51	0.0	0	1.18	0.0	2	0.77	2.6	1	0.72	1.4	3	3.17	0.9
Corpus uteri	0	0.27	0.0	0	0.53	0.0	0	0.34	0.0	0	0.40	0.0	0	1.54	0.0
Uterus, NOS	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.09	0.0
Ovary, fallopian tubes	0	0.30	0.0	0	0.62	0.0	0	0.40	0.0	0	0.44	0.0	0	1.75	0.0
Prostate gland	0	0.70	0.0	0	1.28	0.0	2	0.79	2.5	1	1.00	1.0	3	3.77	0.8
Testis	0	0.14	0.0	1	0.36	2.7	1	0.23	4.4	0	0.16	0.0	2	0.90	2.2
Kidney, renal pelvis, ureter	0	0.34	0.0	3	0.67	4.5	1	0.42	2.4	1	0.48	2.1	5	1.92	2.6
Bladder, other urinary	0	0.67	0.0	1	1.30	0.8	6	0.81	7.4[b]	7	0.96	7.3[b]	14	3.73	3.8[b]
Melanoma of the skin	0	0.18	0.0	0	0.44	0.0	0	0.32	0.0	1	0.31	3.2	1	1.26	0.8
Eye	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.22	0.0
Brain, central nervous system	0	0.33	0.0	1	0.69	1.4	1	0.43	2.3	2	0.41	4.9	4	1.87	2.1
Thyroid gland	0	0.05	0.0	0	0.12	0.0	0	0.08	0.0	1	0.07	14.3	1	0.32	3.1
Bone	0	0.03	0.0	0	0.07	0.0	0	0.03	0.0	1	0.03	33.3	1	0.18	5.6
Connective tissue	0	0.05	0.0	0	0.11	0.0	0	0.07	0.0	0	0.05	0.0	0	0.29	0.0
Lymphatic, hematopoietic system	**2**	**0.80**	**2.5**	**5**	**1.58**	**3.2**[b]	**7**	**0.95**	**7.4**[b]	**4**	**0.96**	**4.2**[b]	**18**	**4.28**	**4.2**[b]
Non-Hodgkin's lymphoma	0	0.21	0.0	0	0.43	0.0	2	0.27	7.4	1	0.28	3.6	3	1.19	2.5
Hodgkin's disease	0	0.12	0.0	0	0.26	0.0	0	0.14	0.0	0	0.10	0.0	0	0.62	0.0
Multiple myeloma	0	0.12	0.0	0	0.23	0.0	0	0.14	0.0	0	0.17	0.0	0	0.66	0.0
Leukemias	2	0.34	5.9	5	0.64	7.8[b]	5	0.39	12.8[b]	3	0.41	7.3[b]	15	1.77	8.5[b]
Chronic lymphocytic	1	0.15	6.7	1	0.26	3.8	0	0.16	0.0	1	0.17	5.9	3	0.73	4.1
Acute nonlymphocytic	1	0.09	11.1	3	0.21	14.3[b]	4	0.13	30.8[b]	2	0.14	14.3[b]	10	0.58	17.2[b]

[a] ICD-7 code = 201.

[b] $P < .05$.

HODGKIN'S DISEASE MALES

TABLE 2D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial Hodgkin's disease among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	2,307			1,610			663			295			2,307		
Person-yr in interval	1,952			4,140			2,254			1,649			9,994		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**6**	**6.90**	**0.9**	**21**	**13.07**	**1.6**	**21**	**7.85**	**2.7**[b]	**16**	**8.84**	**1.8**[b]	**64**	**36.67**	**1.7**[b]
All excluding site of initial cancer	**6**	**6.82**	**0.9**	**21**	**12.90**	**1.6**[b]	**21**	**7.76**	**2.7**[b]	**16**	**8.77**	**1.8**[b]	**64**	**36.26**	**1.8**[b]
Buccal cavity, pharynx	**0**	**0.26**	**0.0**	**0**	**0.48**	**0.0**	**1**	**0.29**	**3.5**	**0**	**0.30**	**0.0**	**1**	**1.32**	**0.8**
Lip	0	0.14	0.0	0	0.26	0.0	0	0.15	0.0	0	0.16	0.0	0	0.71	0.0
Tongue	0	0.02	0.0	0	0.03	0.0	1	0.02	48.0	0	0.02	0.0	1	0.09	10.6
Salivary gland	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.02	0.0	0	0.12	0.0
Gum, other mouth	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.04	0.0	0	0.17	0.0
Pharynx	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	0	0.05	0.0	0	0.23	0.0
Digestive system	**1**	**2.37**	**0.4**	**7**	**4.20**	**1.7**	**4**	**2.46**	**1.6**	**5**	**2.77**	**1.8**	**17**	**11.80**	**1.4**
Esophagus	0	0.11	0.0	0	0.18	0.0	0	0.11	0.0	1	0.12	8.6	1	0.51	2.0
Stomach	0	0.73	0.0	3	1.20	2.5	2	0.67	3.0	0	0.70	0.0	5	3.30	1.5
Colon	1	0.53	1.9	1	0.98	1.0	0	0.60	0.0	0	0.71	0.0	2	2.82	0.7
Rectum	0	0.54	0.0	1	0.96	1.0	0	0.56	0.0	2	0.62	3.2	3	2.67	1.1
Liver, biliary	0	0.13	0.0	2	0.24	8.2	0	0.15	0.0	0	0.18	0.0	2	0.71	2.8
Pancreas	0	0.26	0.0	0	0.48	0.0	2	0.29	6.9	2	0.34	5.8	4	1.37	2.9
Respiratory system	**4**	**1.49**	**2.7**	**5**	**2.91**	**1.7**	**5**	**1.76**	**2.8**	**5**	**2.09**	**2.4**	**19**	**8.25**	**2.3**[b]
Nasal cavities, sinuses	0	0.02	0.0	1	0.04	24.5	0	0.03	0.0	0	0.03	0.0	1	0.11	8.7
Larynx	0	0.11	0.0	0	0.22	0.0	1	0.14	7.3	0	0.15	0.0	1	0.62	1.6
Trachea, bronchus, lung	4	1.29	3.1	4	2.54	1.6	4	1.53	2.6	5	1.83	2.7	17	7.19	2.4[b]
Prostate gland	0	0.70	0.0	0	1.28	0.0	2	0.79	2.5	1	1.00	1.0	3	3.77	0.8
Testis	0	0.14	0.0	1	0.36	2.7	1	0.23	4.4	0	0.16	0.0	2	0.90	2.2
Kidney, renal pelvis, ureter	0	0.23	0.0	2	0.45	4.4	1	0.28	3.6	0	0.32	0.0	3	1.28	2.3
Bladder, other urinary	0	0.55	0.0	1	1.08	0.9	2	0.67	3.0	4	0.80	5.0[b]	7	3.09	2.3
Melanoma of the skin	0	0.09	0.0	0	0.22	0.0	0	0.15	0.0	0	0.14	0.0	0	0.60	0.0
Eye	0	0.03	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.14	0.0
Brain, central nervous system	0	0.21	0.0	0	0.42	0.0	1	0.25	4.0	0	0.23	0.0	1	1.11	0.9
Thyroid gland	0	0.02	0.0	0	0.05	0.0	0	0.03	0.0	0	0.03	0.0	0	0.13	0.0
Bone	0	0.02	0.0	0	0.05	0.0	0	0.02	0.0	0	0.02	0.0	0	0.12	0.0
Connective tissue	0	0.03	0.0	0	0.07	0.0	0	0.04	0.0	0	0.03	0.0	0	0.18	0.0
Lymphatic, hematopoietic system	**1**	**0.54**	**1.9**	**5**	**1.05**	**4.8**[b]	**4**	**0.62**	**6.5**[b]	**1**	**0.64**	**1.6**	**11**	**2.84**	**3.9**[b]
Non-Hodgkin's lymphoma	0	0.14	0.0	0	0.28	0.0	1	0.17	5.9	0	0.18	0.0	1	0.77	1.3
Hodgkin's disease	0	0.08	0.0	0	0.17	0.0	0	0.09	0.0	0	0.07	0.0	0	0.41	0.0
Multiple myeloma	0	0.08	0.0	0	0.15	0.0	0	0.09	0.0	0	0.11	0.0	0	0.43	0.0
Leukemias	1	0.23	4.4	5	0.43	11.5[b]	3	0.26	11.6[b]	1	0.28	3.6	10	1.20	8.4[b]
Chronic lymphocytic	1	0.11	9.4	1	0.19	5.2	0	0.12	0.0	0	0.13	0.0	2	0.54	3.7
Acute nonlymphocytic	0	0.06	0.0	3	0.13	23.1[b]	3	0.08	38.4[b]	1	0.09	11.7	7	0.36	19.7[b]

[a] ICD-7 code = 201.

[b] $P < .05$.

HODGKIN'S DISEASE
FEMALES

TABLE 2E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial Hodgkin's disease among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,542			1,128			539			239			1,542		
Person-yr in interval	1,325			3,094			1,873			1,392			7,685		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4**	**4.77**	**0.8**	**6**	**9.61**	**0.6**	**13**	**6.24**	**2.1**[b]	**18**	**6.49**	**2.8**[b]	**41**	**27.11**	**1.5**[b]
All excluding site of initial cancer	**4**	**4.73**	**0.8**	**6**	**9.52**	**0.6**	**13**	**6.19**	**2.1**[b]	**18**	**6.46**	**2.8**[b]	**41**	**26.90**	**1.5**[b]
Buccal cavity, pharynx	**0**	**0.06**	**0.0**	**0**	**0.12**	**0.0**	**0**	**0.08**	**0.0**	**1**	**0.07**	**13.5**	**1**	**0.33**	**3.0**
Lip	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Tongue	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	0	0.01	0.0	0	0.05	0.0
Salivary gland	0	0.02	0.0	0	0.04	0.0	0	0.02	0.0	0	0.02	0.0	0	0.09	0.0
Gum, other mouth	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Pharynx	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	1	0.02	61.6	1	0.07	15.4
Digestive system	**1**	**1.35**	**0.7**	**3**	**2.42**	**1.2**	**1**	**1.48**	**0.7**	**0**	**1.46**	**0.0**	**5**	**6.70**	**0.7**
Esophagus	0	0.03	0.0	0	0.06	0.0	0	0.04	0.0	0	0.03	0.0	0	0.16	0.0
Stomach	0	0.32	0.0	0	0.51	0.0	0	0.29	0.0	0	0.24	0.0	0	1.36	0.0
Colon	0	0.43	0.0	2	0.81	2.5	0	0.52	0.0	0	0.53	0.0	2	2.29	0.9
Rectum	0	0.25	0.0	0	0.46	0.0	1	0.28	3.6	0	0.29	0.0	1	1.28	0.8
Liver, biliary	0	0.12	0.0	0	0.22	0.0	0	0.13	0.0	0	0.14	0.0	0	0.60	0.0
Pancreas	1	0.14	7.2	1	0.26	3.8	0	0.16	0.0	0	0.18	0.0	2	0.74	2.7
Respiratory system	**0**	**0.23**	**0.0**	**1**	**0.48**	**2.1**	**3**	**0.33**	**9.2**[b]	**0**	**0.40**	**0.0**	**4**	**1.43**	**2.8**
Nasal cavities, sinuses	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.01	0.0	0	0.04	0.0
Larynx	0	0.01	0.0	0	0.02	0.0	0	0.02	0.0	0	0.02	0.0	0	0.07	0.0
Trachea, bronchus, lung	0	0.19	0.0	1	0.41	2.5	3	0.28	10.6[b]	0	0.35	0.0	4	1.23	3.3
Female breast	2	1.06	1.9	0	2.24	0.0	0	1.53	0.0	4	1.69	2.4	6	6.51	0.9
Female genital tract	**0**	**1.15**	**0.0**	**0**	**2.46**	**0.0**	**2**	**1.60**	**1.3**	**1**	**1.63**	**0.6**	**3**	**6.84**	**0.4**
Cervix uteri	0	0.51	0.0	0	1.18	0.0	2	0.77	2.6	1	0.72	1.4	3	3.17	0.9
Corpus uteri	0	0.27	0.0	0	0.53	0.0	0	0.34	0.0	0	0.40	0.0	0	1.54	0.0
Uterus, NOS	0	0.02	0.0	0	0.03	0.0	0	0.02	0.0	0	0.01	0.0	0	0.09	0.0
Ovary, fallopian tubes	0	0.30	0.0	0	0.62	0.0	0	0.40	0.0	0	0.44	0.0	0	1.75	0.0
Kidney, renal pelvis, ureter	0	0.11	0.0	1	0.22	4.5	0	0.14	0.0	1	0.16	6.3	2	0.64	3.1
Bladder, other urinary	0	0.12	0.0	0	0.22	0.0	4	0.14	28.0[b]	3	0.16	19.0[b]	7	0.64	10.9[b]
Melanoma of the skin	0	0.09	0.0	0	0.22	0.0	0	0.17	0.0	1	0.17	5.7	1	0.66	1.5
Eye	0	0.01	0.0	0	0.03	0.0	0	0.02	0.0	0	0.02	0.0	0	0.08	0.0
Brain, central nervous system	0	0.12	0.0	1	0.27	3.6	0	0.18	0.0	2	0.18	10.9[b]	3	0.76	3.9
Thyroid gland	0	0.03	0.0	0	0.07	0.0	0	0.05	0.0	1	0.04	23.1	1	0.19	5.1
Bone	0	0.01	0.0	0	0.02	0.0	0	0.01	0.0	1	0.01	109.4[b]	1	0.06	17.7
Connective tissue	0	0.02	0.0	0	0.04	0.0	0	0.03	0.0	0	0.02	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**1**	**0.26**	**3.8**	**0**	**0.53**	**0.0**	**3**	**0.33**	**9.1**[b]	**3**	**0.32**	**9.4**[b]	**7**	**1.44**	**4.9**[b]
Non-Hodgkin's lymphoma	0	0.07	0.0	0	0.15	0.0	1	0.10	10.3	1	0.10	9.9	2	0.42	4.8
Hodgkin's disease	0	0.04	0.0	0	0.09	0.0	0	0.05	0.0	0	0.03	0.0	0	0.21	0.0
Multiple myeloma	0	0.04	0.0	0	0.08	0.0	0	0.05	0.0	0	0.06	0.0	0	0.23	0.0
Leukemias	1	0.11	9.4	0	0.21	0.0	2	0.13	15.4[b]	2	0.13	15.9[b]	5	0.57	8.7[b]
Chronic lymphocytic	0	0.04	0.0	0	0.07	0.0	0	0.04	0.0	1	0.04	24.2	1	0.19	5.2
Acute nonlymphocytic	1	0.03	28.8	0	0.08	0.0	1	0.05	19.6	1	0.05	18.8	3	0.22	13.9[b]

[a] ICD-7 code = 201.

[b] $P < .05$.

MULTIPLE MYELOMA
BOTH SEXES

TABLE 3A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial multiple myeloma, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	1,867	1,615	3,482
No. who developed a second primary cancer	45	23	68
Average age at diagnosis of first cancer, yr	65	67	66
Average yr of diagnosis of first cancer	1967	1967	1967
Person-yr of follow-up	3,882	3,566	7,448
Average follow-up, yr	2.1	2.2	2.1
Percent given radiotherapy for first cancer	28	28	28

[a] ICD-7 code = 203.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 3B.—*Microscopic confirmation among persons who developed second primary cancers after an initial multiple myeloma in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	51	75.0
Only the first cancer	9	13.2
Only the second cancer	5	7.4
Neither first nor second cancer	3	4.4
Total second primary cancers	68	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

MULTIPLE MYELOMA
BOTH SEXES

TABLE 3C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial multiple myeloma among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	3,482			1,849			376			104			3,482		
Person-yr in interval	2,555			3,404			1,002			487			7,448		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**22**	**28.53**	**0.8**	**30**	**39.61**	**0.8**	**7**	**12.80**	**0.5**	**9**	**6.99**	**1.3**	**68**	**87.95**	**0.8**[b]
All excluding site of initial cancer	**22**	**28.19**	**0.8**	**30**	**39.12**	**0.8**	**7**	**12.64**	**0.6**	**9**	**6.90**	**1.3**	**68**	**86.87**	**0.8**[b]
Buccal cavity, pharynx	**0**	**0.68**	**0.0**	**1**	**0.91**	**1.1**	**0**	**0.29**	**0.0**	**0**	**0.15**	**0.0**	**1**	**2.02**	**0.5**
Lip	0	0.30	0.0	1	0.41	2.4	0	0.13	0.0	0	0.06	0.0	1	0.90	1.1
Tongue	0	0.07	0.0	0	0.09	0.0	0	0.03	0.0	0	0.02	0.0	0	0.20	0.0
Salivary gland	0	0.07	0.0	0	0.11	0.0	0	0.03	0.0	0	0.02	0.0	0	0.23	0.0
Gum, other mouth	0	0.12	0.0	0	0.17	0.0	0	0.05	0.0	0	0.04	0.0	0	0.38	0.0
Pharynx	0	0.11	0.0	0	0.15	0.0	0	0.05	0.0	0	0.03	0.0	0	0.33	0.0
Digestive system	**6**	**10.33**	**0.6**	**7**	**14.04**	**0.5**	**2**	**4.59**	**0.4**	**2**	**2.54**	**0.8**	**17**	**31.49**	**0.5**[b]
Esophagus	0	0.37	0.0	0	0.50	0.0	0	0.17	0.0	1	0.09	11.1	1	1.14	0.9
Stomach	2	2.91	0.7	2	3.70	0.5	1	1.18	0.8	0	0.62	0.0	5	8.42	0.6
Colon	2	2.74	0.7	3	3.88	0.8	1	1.30	0.8	0	0.75	0.0	6	8.68	0.7
Rectum	0	2.11	0.0	2	2.85	0.7	0	0.92	0.0	0	0.49	0.0	2	6.38	0.3
Liver, biliary	0	0.73	0.0	0	1.06	0.0	0	0.36	0.0	0	0.21	0.0	0	2.36	0.0
Pancreas	2	1.11	1.8	0	1.57	0.0	0	0.53	0.0	1	0.29	3.4	3	3.50	0.9
Respiratory system	**3**	**4.16**	**0.7**	**7**	**5.94**	**1.2**	**2**	**1.97**	**1.0**	**2**	**0.98**	**2.0**	**14**	**13.06**	**1.1**
Nasal cavities, sinuses	0	0.07	0.0	0	0.09	0.0	0	0.03	0.0	0	0.01	0.0	0	0.20	0.0
Larynx	0	0.25	0.0	0	0.37	0.0	0	0.12	0.0	0	0.06	0.0	0	0.81	0.0
Trachea, bronchus, lung	3	3.64	0.8	7	5.20	1.3	2	1.73	1.2	2	0.86	2.3	14	11.43	1.2
Female breast	2	2.38	0.8	2	3.41	0.6	0	1.03	0.0	0	0.63	0.0	4	7.46	0.5
Female genital tract	**1**	**2.11**	**0.5**	**0**	**2.99**	**0.0**	**0**	**0.84**	**0.0**	**0**	**0.50**	**0.0**	**1**	**6.45**	**0.2**[b]
Cervix uteri	0	0.62	0.0	0	0.84	0.0	0	0.22	0.0	0	0.13	0.0	0	1.80	0.0
Corpus uteri	0	0.64	0.0	0	0.92	0.0	0	0.26	0.0	0	0.15	0.0	0	1.98	0.0
Uterus, NOS	0	0.05	0.0	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	0	0.14	0.0
Ovary, fallopian tubes	1	0.66	1.5	0	0.95	0.0	0	0.27	0.0	0	0.17	0.0	1	2.05	0.5
Prostate gland	1	2.33	0.4	2	3.18	0.6	1	1.08	0.9	0	0.58	0.0	4	7.17	0.6
Testis	0	0.05	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.16	0.0
Kidney, renal pelvis, ureter	4	0.87	4.6[b]	3	1.23	2.4	1	0.41	2.4	0	0.22	0.0	8	2.74	2.9[b]
Bladder, other urinary	0	1.75	0.0	1	2.49	0.4	1	0.84	1.2	1	0.45	2.2	3	5.52	0.5
Melanoma of the skin	0	0.29	0.0	0	0.42	0.0	0	0.13	0.0	1	0.07	14.3	1	0.91	1.1
Eye	0	0.08	0.0	0	0.12	0.0	0	0.03	0.0	0	0.02	0.0	0	0.25	0.0
Brain, central nervous system	2	0.49	4.1	2	0.69	2.9	0	0.21	0.0	1	0.10	10.0	5	1.49	3.4[b]
Thyroid gland	0	0.13	0.0	1	0.18	5.6	0	0.06	0.0	0	0.03	0.0	1	0.40	2.5
Bone	0	0.05	0.0	0	0.07	0.0	0	0.02	0.0	0	0.02	0.0	0	0.14	0.0
Connective tissue	0	0.09	0.0	0	0.12	0.0	0	0.03	0.0	0	0.02	0.0	0	0.27	0.0
Lymphatic, hematopoietic system	**2**	**1.75**	**1.1**	**4**	**2.44**	**1.6**	**0**	**0.80**	**0.0**	**2**	**0.43**	**4.7**	**8**	**5.43**	**1.5**
Non-Hodgkin's lymphoma	0	0.47	0.0	0	0.68	0.0	0	0.22	0.0	2	0.12	16.7[b]	2	1.49	1.3
Hodgkin's disease	0	0.12	0.0	0	0.16	0.0	0	0.05	0.0	0	0.02	0.0	0	0.35	0.0
Multiple myeloma	0	0.34	0.0	0	0.49	0.0	0	0.16	0.0	0	0.09	0.0	0	1.08	0.0
Leukemias	2	0.79	2.5	4	1.10	3.6	0	0.37	0.0	0	0.20	0.0	6	2.44	2.5
Chronic lymphocytic	0	0.41	0.0	0	0.57	0.0	0	0.19	0.0	0	0.11	0.0	0	1.27	0.0
Acute nonlymphocytic	2	0.21	9.5[b]	4	0.30	13.3[b]	0	0.10	0.0	0	0.05	0.0	6	0.66	9.1[b]

[a] ICD-7 code = 203.

[b] $P < .05$.

MULTIPLE MYELOMA
MALES

TABLE 3D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial multiple myeloma among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,867			985			198			56			1,867		
Person-yr in interval	1,363			1,757			545			217			3,882		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**11**	**16.79**	**0.7**	**22**	**22.77**	**1.0**	**5**	**7.57**	**0.7**	**7**	**3.73**	**1.9**	**45**	**50.87**	**0.9**
All excluding site of initial cancer	**11**	**16.58**	**0.7**	**22**	**22.48**	**1.0**	**5**	**7.47**	**0.7**	**7**	**3.68**	**1.9**	**45**	**50.22**	**0.9**
Buccal cavity, pharynx	**0**	**0.52**	**0.0**	**1**	**0.68**	**1.5**	**0**	**0.22**	**0.0**	**0**	**0.10**	**0.0**	**1**	**1.52**	**0.7**
Lip	0	0.28	0.0	1	0.37	2.7	0	0.12	0.0	0	0.05	0.0	1	0.82	1.2
Tongue	0	0.04	0.0	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.11	0.0
Salivary gland	0	0.04	0.0	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	0	0.13	0.0
Gum, other mouth	0	0.07	0.0	0	0.10	0.0	0	0.03	0.0	0	0.02	0.0	0	0.23	0.0
Pharynx	0	0.08	0.0	0	0.11	0.0	0	0.04	0.0	0	0.02	0.0	0	0.24	0.0
Digestive system	**4**	**6.17**	**0.6**	**4**	**8.11**	**0.5**	**1**	**2.64**	**0.4**	**1**	**1.30**	**0.8**	**10**	**18.22**	**0.5**
Esophagus	0	0.26	0.0	0	0.34	0.0	0	0.11	0.0	1	0.05	19.6	1	0.77	1.3
Stomach	2	1.88	1.1	1	2.33	0.4	1	0.72	1.4	0	0.34	0.0	4	5.28	0.8
Colon	1	1.43	0.7	1	1.96	0.5	0	0.66	0.0	0	0.34	0.0	2	4.39	0.5
Rectum	0	1.38	0.0	2	1.81	1.1	0	0.59	0.0	0	0.28	0.0	2	4.07	0.5
Liver, biliary	0	0.36	0.0	0	0.50	0.0	0	0.17	0.0	0	0.09	0.0	0	1.12	0.0
Pancreas	1	0.67	1.5	0	0.92	0.0	0	0.32	0.0	0	0.15	0.0	1	2.06	0.5
Respiratory system	**2**	**3.53**	**0.6**	**7**	**4.98**	**1.4**	**2**	**1.68**	**1.2**	**2**	**0.80**	**2.5**	**13**	**11.00**	**1.2**
Nasal cavities, sinuses	0	0.05	0.0	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	0	0.14	0.0
Larynx	0	0.23	0.0	0	0.33	0.0	0	0.11	0.0	0	0.05	0.0	0	0.73	0.0
Trachea, bronchus, lung	2	3.10	0.6	7	4.38	1.6	2	1.48	1.3	2	0.71	2.8	13	9.67	1.3
Prostate gland	1	2.33	0.4	2	3.18	0.6	1	1.08	0.9	0	0.58	0.0	4	7.17	0.6
Testis	0	0.05	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.16	0.0
Kidney, renal pelvis, ureter	3	0.55	5.4[b]	2	0.76	2.6	0	0.26	0.0	0	0.13	0.0	5	1.71	2.9
Bladder, other urinary	0	1.40	0.0	0	1.97	0.0	1	0.67	1.5	1	0.34	3.0	2	4.38	0.5
Melanoma of the skin	0	0.14	0.0	0	0.19	0.0	0	0.06	0.0	1	0.03	32.9	1	0.43	2.3
Eye	0	0.05	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.15	0.0
Brain, central nervous system	0	0.27	0.0	2	0.37	5.4	0	0.12	0.0	0	0.05	0.0	2	0.81	2.5
Thyroid gland	0	0.05	0.0	1	0.06	15.6	0	0.02	0.0	0	0.01	0.0	1	0.14	7.0
Bone	0	0.03	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Connective tissue	0	0.05	0.0	0	0.07	0.0	0	0.02	0.0	0	0.01	0.0	0	0.16	0.0
Lymphatic, hematopoietic system	**1**	**1.10**	**0.9**	**3**	**1.49**	**2.0**	**0**	**0.50**	**0.0**	**2**	**0.24**	**8.3**	**6**	**3.34**	**1.8**
Non-Hodgkin's lymphoma	0	0.28	0.0	0	0.39	0.0	0	0.13	0.0	2	0.06	31.6[b]	2	0.86	2.3
Hodgkin's disease	0	0.08	0.0	0	0.10	0.0	0	0.03	0.0	0	0.01	0.0	0	0.22	0.0
Multiple myeloma	0	0.21	0.0	0	0.29	0.0	0	0.10	0.0	0	0.05	0.0	0	0.65	0.0
Leukemias	1	0.52	1.9	3	0.70	4.3	0	0.24	0.0	0	0.12	0.0	4	1.57	2.5
Chronic lymphocytic	0	0.29	0.0	0	0.39	0.0	0	0.13	0.0	0	0.07	0.0	0	0.87	0.0
Acute nonlymphocytic	1	0.13	7.9	3	0.18	16.6[b]	0	0.06	0.0	0	0.03	0.0	4	0.40	10.1[b]

[a] ICD-7 code = 203.

[b] $P < .05$.

MULTIPLE MYELOMA
FEMALES

Table 3E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial multiple myeloma among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	1,615			864			178			48			1,615		
Person-yr in interval	1,192			1,648			457			270			3,566		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**11**	**11.74**	**0.9**	**8**	**16.84**	**0.5**[b]	**2**	**5.23**	**0.4**	**2**	**3.26**	**0.6**	**23**	**37.08**	**0.6**[b]
All excluding site of initial cancer	**11**	**11.61**	**0.9**	**8**	**16.64**	**0.5**[b]	**2**	**5.17**	**0.4**	**2**	**3.22**	**0.6**	**23**	**36.65**	**0.6**[b]
Buccal cavity, pharynx	**0**	**0.16**	**0.0**	**0**	**0.23**	**0.0**	**0**	**0.07**	**0.0**	**0**	**0.05**	**0.0**	**0**	**0.50**	**0.0**
Lip	0	0.02	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Tongue	0	0.03	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Salivary gland	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Gum, other mouth	0	0.05	0.0	0	0.07	0.0	0	0.02	0.0	0	0.02	0.0	0	0.15	0.0
Pharynx	0	0.03	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.09	0.0
Digestive system	**2**	**4.16**	**0.5**	**3**	**5.93**	**0.5**	**1**	**1.95**	**0.5**	**1**	**1.24**	**0.8**	**7**	**13.27**	**0.5**
Esophagus	0	0.11	0.0	0	0.16	0.0	0	0.06	0.0	0	0.04	0.0	0	0.37	0.0
Stomach	0	1.03	0.0	1	1.37	0.7	0	0.46	0.0	0	0.28	0.0	1	3.14	0.3
Colon	1	1.31	0.8	2	1.92	1.0	1	0.64	1.6	0	0.41	0.0	4	4.29	0.9
Rectum	0	0.73	0.0	0	1.04	0.0	0	0.33	0.0	0	0.21	0.0	0	2.31	0.0
Liver, biliary	0	0.37	0.0	0	0.56	0.0	0	0.19	0.0	0	0.12	0.0	0	1.24	0.0
Pancreas	1	0.44	2.3	0	0.65	0.0	0	0.21	0.0	1	0.14	7.1	2	1.44	1.4
Respiratory system	**1**	**0.63**	**1.6**	**0**	**0.96**	**0.0**	**0**	**0.29**	**0.0**	**0**	**0.18**	**0.0**	**1**	**2.06**	**0.5**
Nasal cavities, sinuses	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.00	0.0	0	0.06	0.0
Larynx	0	0.02	0.0	0	0.04	0.0	0	0.01	0.0	0	0.01	0.0	0	0.08	0.0
Trachea, bronchus, lung	1	0.54	1.9	0	0.82	0.0	0	0.25	0.0	0	0.15	0.0	1	1.76	0.6
Female breast	2	2.38	0.8	2	3.41	0.6	0	1.03	0.0	0	0.63	0.0	4	7.46	0.5
Female genital tract	**1**	**2.11**	**0.5**	**0**	**2.99**	**0.0**	**0**	**0.84**	**0.0**	**0**	**0.50**	**0.0**	**1**	**6.45**	**0.2**[b]
Cervix uteri	0	0.62	0.0	0	0.84	0.0	0	0.22	0.0	0	0.13	0.0	0	1.80	0.0
Corpus uteri	0	0.64	0.0	0	0.92	0.0	0	0.26	0.0	0	0.15	0.0	0	1.98	0.0
Uterus, NOS	0	0.05	0.0	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	0	0.14	0.0
Ovary, fallopian tubes	1	0.66	1.5	0	0.95	0.0	0	0.27	0.0	0	0.17	0.0	1	2.05	0.5
Kidney, renal pelvis, ureter	1	0.32	3.1	1	0.47	2.1	1	0.15	6.8	0	0.09	0.0	3	1.03	2.9
Bladder, other urinary	0	0.35	0.0	1	0.52	1.9	0	0.17	0.0	0	0.11	0.0	1	1.14	0.9
Melanoma of the skin	0	0.15	0.0	0	0.23	0.0	0	0.07	0.0	0	0.04	0.0	0	0.48	0.0
Eye	0	0.03	0.0	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	0	0.10	0.0
Brain, central nervous system	2	0.22	9.1[b]	0	0.32	0.0	0	0.09	0.0	1	0.05	18.7	3	0.68	4.4
Thyroid gland	0	0.08	0.0	0	0.12	0.0	0	0.04	0.0	0	0.02	0.0	0	0.26	0.0
Bone	0	0.02	0.0	0	0.03	0.0	0	0.01	0.0	0	0.01	0.0	0	0.06	0.0
Connective tissue	0	0.04	0.0	0	0.05	0.0	0	0.01	0.0	0	0.01	0.0	0	0.11	0.0
Lymphatic, hematopoietic system	**1**	**0.65**	**1.5**	**1**	**0.95**	**1.1**	**0**	**0.30**	**0.0**	**0**	**0.19**	**0.0**	**2**	**2.09**	**1.0**
Non-Hodgkin's lymphoma	0	0.19	0.0	0	0.29	0.0	0	0.09	0.0	0	0.06	0.0	0	0.63	0.0
Hodgkin's disease	0	0.04	0.0	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	0	0.13	0.0
Multiple myeloma	0	0.13	0.0	0	0.20	0.0	0	0.06	0.0	0	0.04	0.0	0	0.43	0.0
Leukemias	1	0.27	3.7	1	0.40	2.5	0	0.13	0.0	0	0.08	0.0	2	0.87	2.3
Chronic lymphocytic	0	0.12	0.0	0	0.18	0.0	0	0.06	0.0	0	0.04	0.0	0	0.40	0.0
Acute nonlymphocytic	1	0.08	12.5	1	0.12	8.2	0	0.04	0.0	0	0.02	0.0	2	0.26	7.6

[a] ICD-7 code = 203.

[b] $P < .05$.

LEUKEMIA
BOTH SEXES

TABLE 4A.—*Characteristics of persons reported to the Danish Cancer Registry with an initial leukemia, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	5,591	3,904	9,495
No. who developed a second primary cancer	152	66	218
Average age at diagnosis of first cancer, yr	54	54	54
Average yr of diagnosis of first cancer	1965	1965	1965
Person-yr of follow-up	11,985	9,183	21,168
Average follow-up, yr	2.1	2.4	2.2
Percent given radiotherapy for first cancer	23	20	22

[a] ICD-7 code = 204.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 4B.—*Microscopic confirmation among persons who developed second primary cancers after an initial leukemia in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	168	77.1
Only the first cancer	29	13.3
Only the second cancer	13	6.0
Neither first nor second cancer	8	3.7
Total second primary cancers	218	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

LEUKEMIA
BOTH SEXES

TABLE 4C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial leukemia among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	9,495			4,987			1,147			293			9,495		
Person-yr in interval	6,868			9,942			2,980			1,378			21,168		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**56**	**60.00**	**0.9**	**98**	**96.80**	**1.0**	**42**	**31.08**	**1.4**	**22**	**17.10**	**1.3**	**218**	**204.98**	**1.1**
All excluding site of initial cancer	**53**	**58.26**	**0.9**	**98**	**94.05**	**1.0**	**42**	**30.21**	**1.4**[b]	**22**	**16.62**	**1.3**	**215**	**199.14**	**1.1**
Buccal cavity, pharynx	**4**	**1.52**	**2.6**	**7**	**2.38**	**2.9**[b]	**1**	**0.72**	**1.4**	**2**	**0.35**	**5.7**	**14**	**4.97**	**2.8**[b]
Lip	2	0.71	2.8	5	1.11	4.5[b]	0	0.31	0.0	0	0.14	0.0	7	2.28	3.1[b]
Tongue	0	0.14	0.0	0	0.22	0.0	0	0.07	0.0	0	0.04	0.0	0	0.48	0.0
Salivary gland	1	0.16	6.3	0	0.26	0.0	0	0.08	0.0	1	0.04	25.0	2	0.54	3.7
Gum, other mouth	0	0.25	0.0	2	0.41	4.9	1	0.13	7.7	0	0.08	0.0	3	0.88	3.4
Pharynx	1	0.24	4.2	0	0.38	0.0	0	0.12	0.0	1	0.06	16.7	2	0.81	2.5
Digestive system	**18**	**22.28**	**0.8**	**27**	**35.23**	**0.8**	**12**	**11.00**	**1.1**	**7**	**6.35**	**1.1**	**64**	**74.86**	**0.9**
Esophagus	1	0.86	1.2	0	1.33	0.0	2	0.39	5.1	0	0.21	0.0	3	2.80	1.1
Stomach	6	6.66	0.9	7	10.05	0.7	0	2.89	0.0	0	1.60	0.0	13	21.20	0.6
Colon	3	5.68	0.5	7	9.24	0.8	6	3.05	2.0	2	1.90	1.1	18	19.87	0.9
Rectum	3	4.60	0.7	10	7.28	1.4	1	2.22	0.5	0	1.21	0.0	14	15.29	0.9
Liver, biliary	2	1.44	1.4	1	2.40	0.4	1	0.83	1.2	3	0.52	5.8[b]	7	5.19	1.3
Pancreas	1	2.26	0.4	2	3.75	0.5	0	1.23	0.0	2	0.72	2.8	5	7.96	0.6
Respiratory system	**5**	**8.76**	**0.6**	**17**	**14.67**	**1.2**	**15**	**4.68**	**3.2**[b]	**0**	**2.18**	**0.0**	**37**	**30.29**	**1.2**
Nasal cavities, sinuses	0	0.14	0.0	1	0.22	4.5	0	0.07	0.0	0	0.03	0.0	1	0.46	2.2
Larynx	0	0.56	0.0	0	0.93	0.0	1	0.29	3.4	0	0.13	0.0	1	1.90	0.5
Trachea, bronchus, lung	5	7.61	0.7	14	12.79	1.1	12	4.10	2.9[b]	0	1.91	0.0	31	26.42	1.2
Female breast	3	4.30	0.7	2	7.07	0.3	0	2.73	0.0	2	1.77	1.1	7	15.86	0.4[b]
Female genital tract	**1**	**3.84**	**0.3**	**1**	**6.27**	**0.2**[b]	**1**	**2.35**	**0.4**	**1**	**1.34**	**0.7**	**4**	**13.79**	**0.3**[b]
Cervix uteri	1	1.21	0.8	1	1.89	0.5	1	0.66	1.5	0	0.34	0.0	3	4.11	0.7
Corpus uteri	0	1.10	0.0	0	1.86	0.0	0	0.71	0.0	0	0.40	0.0	0	4.08	0.0[b]
Uterus, NOS	0	0.09	0.0	0	0.14	0.0	0	0.05	0.0	0	0.04	0.0	0	0.33	0.0
Ovary, fallopian tubes	0	1.16	0.0	0	1.93	0.0	0	0.75	0.0	1	0.43	2.3	1	4.27	0.2
Prostate gland	4	5.39	0.7	17	8.65	2.0[b]	3	2.40	1.3	1	1.22	0.8	25	17.66	1.4
Testis	0	0.17	0.0	0	0.24	0.0	0	0.07	0.0	0	0.03	0.0	0	0.51	0.0
Kidney, renal pelvis, ureter	4	1.82	2.2	12	2.98	4.0[b]	1	0.96	1.0	1	0.52	1.9	18	6.28	2.9[b]
Bladder, other urinary	5	3.70	1.4	5	6.16	0.8	1	1.95	0.5	4	0.99	4.0[b]	15	12.82	1.2
Melanoma of the skin	1	0.59	1.7	1	0.96	1.0	2	0.34	5.9	1	0.18	5.6	5	2.06	2.4
Eye	0	0.18	0.0	0	0.29	0.0	0	0.09	0.0	0	0.04	0.0	0	0.59	0.0
Brain, central nervous system	3	1.04	2.9	1	1.67	0.6	0	0.55	0.0	0	0.26	0.0	4	3.51	1.1
Thyroid gland	0	0.26	0.0	0	0.42	0.0	0	0.15	0.0	0	0.09	0.0	0	0.91	0.0
Bone	0	0.12	0.0	0	0.17	0.0	0	0.05	0.0	1	0.02	50.0	1	0.36	2.8
Connective tissue	1	0.21	4.8	1	0.32	3.1	1	0.09	11.1	0	0.04	0.0	3	0.67	4.5
Lymphatic, hematopoietic system	**6**	**3.73**	**1.6**	**5**	**6.00**	**0.8**	**3**	**1.92**	**1.6**	**2**	**1.06**	**1.9**	**16**	**12.70**	**1.3**
Non-Hodgkin's lymphoma	3	0.99	3.0	1	1.61	0.6	3	0.53	5.7[b]	2	0.30	6.7	9	3.43	2.6[b]
Hodgkin's disease	0	0.27	0.0	3	0.42	7.1[b]	0	0.13	0.0	0	0.06	0.0	3	0.88	3.4
Multiple myeloma	0	0.70	0.0	1	1.15	0.9	0	0.38	0.0	0	0.21	0.0	1	2.43	0.4
Leukemias	3	1.74	1.7	0	2.75	0.0	0	0.87	0.0	0	0.48	0.0	3	5.84	0.5
Chronic lymphocytic	1	0.90	1.1	0	1.43	0.0	0	0.44	0.0	0	0.25	0.0	1	3.02	0.3
Acute nonlymphocytic	2	0.43	4.7	0	0.70	0.0	0	0.24	0.0	0	0.14	0.0	2	1.51	1.3

[a] ICD-7 code = 204.

[b] $P < .05$.

LEUKEMIA
MALES

TABLE 4D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial leukemia among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	5,591			2,949			630			143			5,591		
Person-yr in interval	4,060			5,765			1,547			614			11,985		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**37**	**38.85**	**1.0**	**70**	**62.00**	**1.1**	**31**	**17.46**	**1.8**[b]	**14**	**8.00**	**1.8**	**152**	**126.31**	**1.2**[b]
All excluding site of initial cancer	**36**	**37.61**	**1.0**	**70**	**60.06**	**1.2**	**31**	**16.92**	**1.8**[b]	**14**	**7.75**	**1.8**	**151**	**122.33**	**1.2**[b]
Buccal cavity, pharynx	**3**	**1.23**	**2.4**	**4**	**1.91**	**2.1**	**0**	**0.53**	**0.0**	**2**	**0.22**	**8.9**[b]	**9**	**3.89**	**2.3**[b]
Lip	2	0.67	3.0	3	1.04	2.9	0	0.28	0.0	0	0.12	0.0	5	2.11	2.4
Tongue	0	0.09	0.0	0	0.14	0.0	0	0.04	0.0	0	0.02	0.0	0	0.29	0.0
Salivary gland	0	0.10	0.0	0	0.16	0.0	0	0.04	0.0	1	0.02	53.8	1	0.32	3.1
Gum, other mouth	0	0.17	0.0	1	0.27	3.7	0	0.08	0.0	0	0.04	0.0	1	0.56	1.8
Pharynx	1	0.19	5.2	0	0.30	0.0	0	0.09	0.0	1	0.04	28.2	2	0.62	3.2
Digestive system	**12**	**14.75**	**0.8**	**14**	**22.89**	**0.6**	**8**	**6.10**	**1.3**	**5**	**2.83**	**1.8**	**39**	**46.57**	**0.8**
Esophagus	0	0.65	0.0	0	0.99	0.0	0	0.26	0.0	0	0.11	0.0	0	2.01	0.0
Stomach	5	4.69	1.1	4	6.96	0.6	0	1.72	0.0	0	0.78	0.0	9	14.16	0.6
Colon	3	3.36	0.9	2	5.36	0.4	5	1.48	3.4[b]	1	0.72	1.4	11	10.92	1.0
Rectum	1	3.29	0.3	6	5.12	1.2	1	1.37	0.7	0	0.63	0.0	8	10.40	0.8
Liver, biliary	1	0.80	1.3	1	1.31	0.8	0	0.38	0.0	3	0.18	16.3[b]	5	2.67	1.9
Pancreas	1	1.51	0.7	1	2.47	0.4	0	0.70	0.0	1	0.33	3.0	3	5.01	0.6
Respiratory system	**5**	**7.69**	**0.7**	**17**	**12.84**	**1.3**	**14**	**3.92**	**3.6**[b]	**0**	**1.68**	**0.0**	**36**	**26.13**	**1.4**
Nasal cavities, sinuses	0	0.11	0.0	1	0.17	5.9	0	0.05	0.0	0	0.02	0.0	1	0.34	2.9
Larynx	0	0.52	0.0	0	0.86	0.0	1	0.26	3.8	0	0.11	0.0	1	1.74	0.6
Trachea, bronchus, lung	5	6.71	0.7	14	11.24	1.2	12	3.45	3.5[b]	0	1.48	0.0	31	22.89	1.4
Prostate gland	4	5.39	0.7	17	8.65	2.0[b]	3	2.40	1.3	1	1.22	0.8	25	17.66	1.4
Testis	0	0.17	0.0	0	0.24	0.0	0	0.07	0.0	0	0.03	0.0	0	0.51	0.0
Kidney, renal pelvis, ureter	3	1.26	2.4	6	2.04	2.9[b]	1	0.58	1.7	1	0.27	3.8	11	4.15	2.6[b]
Bladder, other urinary	4	3.11	1.3	5	5.15	1.0	1	1.53	0.7	3	0.70	4.3	13	10.50	1.2
Melanoma of the skin	1	0.32	3.2	1	0.51	2.0	1	0.16	6.4	0	0.07	0.0	3	1.05	2.9
Eye	0	0.12	0.0	0	0.19	0.0	0	0.05	0.0	0	0.02	0.0	0	0.38	0.0
Brain, central nervous system	2	0.64	3.1	1	1.01	1.0	0	0.30	0.0	0	0.12	0.0	3	2.06	1.5
Thyroid gland	0	0.11	0.0	0	0.18	0.0	0	0.05	0.0	0	0.02	0.0	0	0.36	0.0
Bone	0	0.08	0.0	0	0.11	0.0	0	0.03	0.0	1	0.01	77.2[b]	1	0.23	4.3
Connective tissue	0	0.14	0.0	0	0.21	0.0	1	0.05	18.4	0	0.02	0.0	1	0.42	2.4
Lymphatic, hematopoietic system	**2**	**2.58**	**0.8**	**4**	**4.09**	**1.0**	**1**	**1.15**	**0.9**	**1**	**0.53**	**1.9**	**8**	**8.34**	**1.0**
Non-Hodgkin's lymphoma	1	0.65	1.5	1	1.05	1.0	1	0.30	3.3	1	0.14	7.4	4	2.14	1.9
Hodgkin's disease	0	0.19	0.0	2	0.29	6.9	0	0.08	0.0	0	0.03	0.0	2	0.59	3.4
Multiple myeloma	0	0.47	0.0	1	0.76	1.3	0	0.22	0.0	0	0.10	0.0	1	1.55	0.6
Leukemias	1	1.24	0.8	0	1.94	0.0	0	0.54	0.0	0	0.25	0.0	1	3.98	0.3
Chronic lymphocytic	0	0.68	0.0	0	1.07	0.0	0	0.29	0.0	0	0.14	0.0	0	2.19	0.0
Acute nonlymphocytic	1	0.29	3.4	0	0.47	0.0	0	0.14	0.0	0	0.07	0.0	1	0.97	1.0

[a] ICD-7 code = 204.

[b] $P < .05$.

LEUKEMIA
FEMALES

TABLE 4E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of an initial leukemia among females in Denmark, 1943-80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1-4 yr			5-9 yr			10+ yr			Total		
No. starting interval	3,904			2,038			517			150			3,904		
Person-yr in interval	2,807			4,178			1,433			764			9,183		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	19	21.15	0.9	28	34.80	0.8	11	13.62	0.8	8	9.10	0.9	66	78.67	0.8
All excluding site of initial cancer	17	20.65	0.8	28	33.99	0.8	11	13.29	0.8	8	8.87	0.9	64	76.81	0.8
Buccal cavity, pharynx	1	0.29	3.5	3	0.47	6.3^b	1	0.19	5.4	0	0.13	0.0	5	1.08	4.6^b
Lip	0	0.04	0.0	2	0.07	27.5^b	0	0.03	0.0	0	0.02	0.0	2	0.17	12.1^b
Tongue	0	0.05	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.19	0.0
Salivary gland	1	0.06	16.3	0	0.10	0.0	0	0.04	0.0	0	0.02	0.0	1	0.22	4.6
Gum, other mouth	0	0.08	0.0	1	0.14	7.3	1	0.05	18.2	0	0.04	0.0	2	0.32	6.3
Pharynx	0	0.05	0.0	0	0.08	0.0	0	0.03	0.0	0	0.02	0.0	0	0.19	0.0
Digestive system	6	7.53	0.8	13	12.34	1.1	4	4.90	0.8	2	3.52	0.6	25	28.29	0.9
Esophagus	1	0.21	4.7	0	0.34	0.0	2	0.13	15.0^b	0	0.10	0.0	3	0.79	3.8
Stomach	1	1.97	0.5	3	3.09	1.0	0	1.17	0.0	0	0.82	0.0	4	7.04	0.6
Colon	0	2.32	0.0	5	3.88	1.3	1	1.57	0.6	1	1.18	0.8	7	8.95	0.8
Rectum	2	1.31	1.5	4	2.16	1.9	0	0.85	0.0	0	0.58	0.0	6	4.89	1.2
Liver, biliary	1	0.64	1.6	0	1.09	0.0	1	0.45	2.2	0	0.34	0.0	2	2.52	0.8
Pancreas	0	0.75	0.0	1	1.28	0.8	0	0.53	0.0	1	0.39	2.6	2	2.95	0.7
Respiratory system	0	1.07	0.0	0	1.83	0.0	1	0.76	1.3	0	0.50	0.0	1	4.16	0.2
Nasal cavities, sinuses	0	0.03	0.0	0	0.05	0.0	0	0.02	0.0	0	0.01	0.0	0	0.12	0.0
Larynx	0	0.04	0.0	0	0.07	0.0	0	0.03	0.0	0	0.02	0.0	0	0.16	0.0
Trachea, bronchus, lung	0	0.90	0.0	0	1.55	0.0	0	0.65	0.0	0	0.43	0.0	0	3.53	0.0
Female breast	3	4.30	0.7	2	7.07	0.3	0	2.73	0.0	2	1.77	1.1	7	15.86	0.4^b
Female genital tract	1	3.84	0.3	1	6.27	0.2^b	1	2.35	0.4	1	1.34	0.7	4	13.79	0.3^b
Cervix uteri	1	1.21	0.8	1	1.89	0.5	1	0.66	1.5	0	0.34	0.0	3	4.11	0.7
Corpus uteri	0	1.10	0.0	0	1.86	0.0	0	0.71	0.0	0	0.40	0.0	0	4.08	0.0^b
Uterus, NOS	0	0.09	0.0	0	0.14	0.0	0	0.05	0.0	0	0.04	0.0	0	0.33	0.0
Ovary, fallopian tubes	0	1.16	0.0	0	1.93	0.0	0	0.75	0.0	1	0.43	2.3	1	4.27	0.2
Kidney, renal pelvis, ureter	1	0.56	1.8	6	0.94	6.4^b	0	0.38	0.0	0	0.25	0.0	7	2.13	3.3^b
Bladder, other urinary	1	0.59	1.7	0	1.01	0.0	0	0.42	0.0	1	0.29	3.4	2	2.32	0.9
Melanoma of the skin	0	0.27	0.0	0	0.45	0.0	1	0.18	5.6	1	0.11	8.9	2	1.01	2.0
Eye	0	0.06	0.0	0	0.10	0.0	0	0.04	0.0	0	0.02	0.0	0	0.21	0.0
Brain, central nervous system	1	0.40	2.5	0	0.66	0.0	0	0.25	0.0	0	0.14	0.0	1	1.45	0.7
Thyroid gland	0	0.15	0.0	0	0.24	0.0	0	0.10	0.0	0	0.07	0.0	0	0.55	0.0
Bone	0	0.04	0.0	0	0.06	0.0	0	0.02	0.0	0	0.01	0.0	0	0.13	0.0
Connective tissue	1	0.07	14.0	1	0.11	8.8	0	0.04	0.0	0	0.02	0.0	2	0.25	7.9
Lymphatic, hematopoietic system	4	1.15	3.5	1	1.91	0.5	2	0.77	2.6	1	0.53	1.9	8	4.36	1.8
Non-Hodgkin's lymphoma	2	0.34	6.0	0	0.56	0.0	2	0.23	8.7	1	0.16	6.3	5	1.29	3.9^b
Hodgkin's disease	0	0.08	0.0	1	0.13	7.5	0	0.05	0.0	0	0.03	0.0	1	0.29	3.4
Multiple myeloma	0	0.23	0.0	0	0.39	0.0	0	0.16	0.0	0	0.11	0.0	0	0.88	0.0
Leukemias	2	0.50	4.0	0	0.81	0.0	0	0.33	0.0	0	0.23	0.0	2	1.86	1.1
Chronic lymphocytic	1	0.22	4.6	0	0.36	0.0	0	0.15	0.0	0	0.11	0.0	1	0.83	1.2
Acute nonlymphocytic	1	0.14	7.0	0	0.23	0.0	0	0.10	0.0	0	0.07	0.0	1	0.54	1.9

[a] ICD-7 code = 204.

[b] $P < .05$.

Summary: Multiple Primary Cancers in Denmark, 1943-80 [1]

Hans H. Storm, Ole M. Jensen, Marianne Ewertz, Elsebeth Lynge, Jørgen H. Olsen,
Geert Schou, *and* Anne Østerlind [2]

ABSTRACT—The risk of developing a second primary cancer was studied among 171,749 men and 208,192 women who were reported to the Danish Cancer Registry between 1943 and 1980. Only those who survived at least 2 months were included in the analysis, and more than 1.7 million person-years of observation were accrued. Altogether, 15,084 second primary cancers developed in organs other than the initial cancer site [relative risk (RR) = 0.99]. Adjustment for possible underreporting of multiple primary cancers increased the RR to 1.06. The overall RR of a second cancer developing for all sites was 0.91, but interpretation of this risk is difficult because new tumors arising within the same organ are generally not recorded in Denmark. The RR for all sites increased with time from 0.94 during the first decade of follow-up (excluding the first year) to 1.13 among 30-year survivors. Patients below the age of 20 years when first diagnosed with cancer experienced significantly increased risks of developing a second cancer. Elevated risks were also observed for sites thought to have a common etiology. For example, cancers of smoking-related sites were increased in both directions for cancers of the oral cavity, respiratory tract, and urinary organs. For cancers suspected to have a hormone- or dietary fat-related association, significant reciprocal relationships were seen among cancers of the endometrium, ovary, and colon. Cancer treatment probably is an important factor in second cancer development, even when judged indirectly in the present study. For example, radiotherapy may have been responsible for an elevated risk of subsequent cancers of the thyroid, breast, colon, rectum, bladder, connective tissue, and hematopoietic system in long-term survivors. Chemotherapy may have increased the risk of subsequent leukemias. Our data further indicate that cancer patients have no general susceptibility to develop new malignant tumors, although high rates may be found for particular sites sharing common risk factors. Conversely, the occurrence of one cancer does not appear to protect against developing a new cancer.—Natl Cancer Inst Monogr 68: 411-430, 1985.

Development of multiple primary cancers in the same individual constitutes a constant challenge to the medical profession and scientists working in cancer research. Should such events be attributed to host susceptibility, could 2 or more cancers be due to the same exogenous risk factor, or were the subsequent cancers induced by previous anticancer therapy? As a prerequisite to rational consideration of such questions, it is necessary that we examine whether the probability of developing a second primary cancer is indeed increased in patients compared with persons without cancer. Furthermore, the risk of subsequent cancer development must be evaluated with regard to tumor site and time elapsed between the first and second primary.

Numerous case reports and studies on multiple primary cancers have appeared since Warren and Gates' review of 430 publications in 1932 (*1*). In a large study reported by Schoenberg (*2*), an overall 29% increased risk of second primary cancers was found among patients who survived their initial cancer. The site and the risk of second primary cancer development varied considerably by index site. Schoenberg's study was based on data collected by the Connecticut Tumor Registry between 1935 and 1964. It showed the usefulness of the population-based cancer registry for the evaluation and quantification of the risk of second primary cancer development. In the present investigation, the risk of second cancers has been examined in Denmark for a 38-year period of cancer registration (*3*). This long follow-up period provides unique opportunities for a population-based study of second cancer development among long-term survivors, in whom risks associated with medical procedures, e.g., radiotherapy, are most likely to be seen. In contrast, etiologic similarities between cancers of different sites, including host susceptibility, are likely to result in increased risks that are not dependent on the duration of survival after the first tumor. Reciprocal associations, i.e., in both directions between sites, would strengthen hypotheses of possible common etiology (*4*).

In this paper, we summarize the results of studies of multiple primary cancers conducted at the Danish Cancer Registry as part of a joint effort with the Connecticut Tumor Registry and the National Cancer Institute (*5-13*). In addition, we describe the risk of second tumor development irrespective of initial primary site and in relation to age at first tumor. The site-specific results dealt with in previous chapters (*5-13*) are combined with a view to possible common risk factors, including risk associated with anticancer treatment of the first primary.

MATERIALS AND METHODS

Cancer registration in Denmark.—Since 1943, incident cases of cancer in Denmark have been reported to the Danish Cancer Registry by hospital departments, pathology institutes, and practicing physicians. Registration is voluntary but, for practical purposes, reporting of initial

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Abbreviations: RR = relative risk(s); CI = confidence interval; ANLL = acute nonlymphocytic leukemia; NHL = non-Hodgkin's lymphoma; CLL = chronic lymphocytic leukemia.

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[1] Prepared in recognition of the Fiftieth Anniversary of the Connecticut Tumor Registry, Department of Health Services, Hartford, Connecticut.

[2] Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Landskronagade 66, DK-2100 Copenhagen, Denmark. *Address reprint requests to* Hans H. Storm, M.D.

cancers may be regarded as complete and valid. However, second primary cancers have been underreported to a certain degree (*3*), especially following hematologic cancers (*13*). Follow-up for vital status is undertaken annually by record linkage with the National Death Registry. During this procedure, any identified cancer cases that were unknown to the Registry are recorded after additional "follow-back" investigations. The Registry contains tumor records that are identified by unique personal identification numbers, which include information on sex and date of birth.

All tumors in the Registry are coded and classified in accordance with a modified version of the Seventh Revision of the International Classification of Diseases (*14*). Multiple primary cancers in the same individual are defined as tumors that arise in different organs or as separate tumors with different morphologic characteristics in the same organ. Before 1979, however, a morphologic distinction within organs was made only between carcinoma and sarcoma. New tumors arising within the same organ are generally not recorded. If 2 or more tumors of the same histologic type arise in paired organs, e.g., kidneys, they are also considered as 1 cancer. Thus examination of the development of a new independent cancer in paired organs was not possible.

Study of multiple primary cancers: 1943–80.—Persons with multiple primary cancers were identified by automated record linkage performed within the Registry. The risk of multiple primary cancer development in persons reported to the Registry was evaluated for the period 1943–80. All nonmelanoma skin cancers, precancerous lesions, and duplicate notifications of the same tumor were excluded.

If a second cancer is diagnosed shortly after referral of a cancer patient to the medical care system, determination of which neoplasm arose first is difficult. Therefore, among 508,026 persons available for study, we included only patients who survived 2 or more months following their initial cancer diagnosis and persons who did not develop a second primary cancer within this 2-month period. A total of 124,646 persons with a single cancer who survived less than 2 months and 3,439 persons with multiple cancers ("simultaneous cancers") were excluded (text-tables 1, 2), leaving 364,857 persons with a single cancer and 15,084 persons with a second primary cancer available for study. A total of 551 third and fourth primary cancers occurred in these individuals but were not considered in this study. A substantial proportion of all registered second primary cancers of the kidney (50%), bladder (30%), prostate (31%), and ovary (30%) were excluded as simultaneous cancers.

Calculation of relative risks.—Person-years at risk were calculated from the date of diagnosis of the first primary cancer (i.e., date of first hospital admission) until the date of diagnosis of a second primary cancer, death, or December 31, 1980, whichever occurred first.

We calculated expected numbers of second primary cancers by multiplying sex, age (5-yr age groups), and calendar period (5-yr), site-specific incidence rates for Denmark by the corresponding person-years at risk using a modified version of the program developed by Monson (*15*). The RR were obtained by division of the observed numbers by the expected numbers calculated over the sex-, age-, and calendar period-specific cells. We computed approximate 95% CI of the RR assuming a Poisson distribution of the observed cancers as described by Rothman and Boice (*16*).

RESULTS AND DISCUSSION

All Primary Sites Combined

Of 379,941 patients, 171,749 men and 208,192 women were diagnosed with cancer between 1943 and 1980 who were eligible for study, and 1,706,736 person-years of observation were accumulated (tables 1A–1H). Second primary cancers developed in 15,084 persons: 4.2% of the women and 3.7% of the men. In persons with multiple tumors, approximately 92% of the first and 85% of the second primary cancers were verified histologically. Only 4% of the second primary cancers were known to the Registry solely from death certificates; death certificate cancer diagnoses are considered less reliable than are cancer diagnoses reported prior to death (*17*). For both sexes combined, 16,580 second primary cancers were expected, yielding a deficit of approximately 1,500 cancers (RR = 0.91; 95% CI = 0.90–0.92). The risk of second primary cancer increased significantly with the time since diagnosis of the first primary ($P < .001$ for trend), from an RR of 0.7 in short-term survivors to 1.0 for persons surviving 10 or more years. Our excluding the first year of observation and stratifying by 10-year intervals since primary cancer diagnosis did not change this trend; the RR rose from 0.94 in years 1–9 to 1.13 among those living 30 or more years after their initial primary cancer.

The overall deficit of second cancers occurred mainly during the first 5 years of follow-up. During this early follow-up period, both the notifying physician and the Registry would be hesitant to accept and record a new primary cancer, and, as a result, a large proportion of such tumors would likely be regarded as misdiagnosed metastases. In addition, the coding practices of the Registry (i.e., 1943–78) in general did not allow for the inclusion of 2 primary cancers at the same site. If the observed and expected second cancers of the same site as the index cancer were subtracted, the RR increased to 0.99 and was not significantly different from unity. Excluding the first 5 years of observation, the RR increased to 1.06 (95% CI = 1.04–1.09). After this adjustment, a slight difference in RR for the sexes emerged (1.08 for women and 1.03 for men, respectively).

The present findings correspond to an annual average incidence of 8.8 second cancers/1,000 persons (7.8/1,000 women; 10.9/1,000 men). For comparison, the annual incidence of second cancer was 7.9/1,000 persons among 41,341 patients at the Memorial Sloan-Kettering Hospital (*18*). Also, 2.8% of 37,580 patients were reported to develop second cancers at the Mayo Clinic (*19*) as compared with 4.0% for our survey. These findings agree well with our results. Higher incidence rates of 12.0/1,000 (15.0/1,000 men; 10.3/1,000 women) were recorded in the study of cancer patients reported to the Connecticut Tumor Registry between 1935 and 1964 (*2*). Although the

TEXT-TABLE 1.—*Number of persons with a single primary cancer who survived less than 2 mo and who were excluded from the analysis, Denmark, 1943–80*

Cancer site/type	Females		Males		Both	
	No.	Percent[a]	No.	Percent[a]	No.	Percent[a]
Lip	13	2.8	62	1.2	75	1.3
Tongue	39	7.2	43	6.7	82	6.9
Salivary gland	33	3.4	52	5.9	85	4.6
Gum, other mouth	56	7.1	58	5.3	114	6.1
Pharynx	80	12.3	153	10.6	233	11.1
Esophagus	706	33.4	1,339	32.5	2,045	32.8
Stomach	8,594	40.9	11,129	37.6	19,723	39.0
Small intestine	237	37.1	277	37.2	514	37.2
Colon	6,480	28.3	5,722	30.4	12,202	29.3
Rectum	2,933	20.8	4,466	22.4	7,399	21.8
Liver, biliary	3,109	52.5	2,593	61.2	5,702	56.1
Pancreas	3,407	48.7	4,324	50.9	7,731	49.9
Nasal cavities	45	11.1	57	7.5	102	8.8
Larynx	47	8.5	179	5.1	226	5.5
Trachea, bronchus, lung	3,609	38.7	15,057	37.3	18,666	37.5
Breast	4,182	7.1	—	—	4,182	7.1
Cervix uteri	1,052	3.8	—	—	1,052	3.8
Corpus uteri	897	6.3	—	—	897	6.3
Ovary	3,084	19.5	—	—	3,084	19.5
Prostate gland	—	—	5,298	21.0	5,298	21.0
Testis	—	—	283	6.2	283	6.2
Kidney, renal pelvis, ureter	1,766	30.4	2,408	32.0	4,174	31.3
Bladder, other urinary	871	15.6	2,178	12.5	3,049	13.2
Melanoma of the skin	175	3.9	186	6.1	361	4.8
Eye	48	5.5	73	7.0	121	6.4
Brain, central nervous system	2,065	29.2	2,208	29.6	4,273	29.4
Thyroid gland	416	23.5	197	25.2	613	24.1
Bone	65	9.1	100	10.1	165	9.7
Connective tissue	86	7.3	115	8.6	201	8.0
Non-Hodgkin's lymphoma	881	23.4	1,159	24.1	2,040	23.8
Hodgkin's disease	241	13.5	345	13.0	586	13.2
Multiple myeloma	623	27.8	845	31.2	1,468	29.7
Leukemias	2,248	36.5	3,147	36.0	5,395	36.2
Other	7,095	40.4	5,410	41.0	12,505	40.6
All sites	55,183	21.0	69,463	28.8	124,646	24.7

[a] For each site, the percent given is the proportion of patients with cancers surviving less than 2 mo of the total number notified to the Registry for that site.

age of the cancer patients, follow-up, treatment practices, registration practices for second cancer, calendar years of study, and so forth, are different between Connecticut and Denmark, it is still important that one notes the significant 29% increased RR of second cancer in Connecticut was not matched by a similar increase in our investigation, even if cases arising during the first 5 years of follow-up are excluded.

A number of explanations could account for the different overall findings between Denmark and Connecticut. The Connecticut Tumor Registry staff actively searches hospital files for cases in addition to receiving notifications from clinicians and information on cancer deaths (*20*). The Danish Cancer Registry relies on physician notification and linkage with death certificates (*3*), which have been found to give a high completeness of reporting (*21, 22*). However, the Danish registration becomes susceptible to local interests, and there are indications that second cancers may be underreported as is true for second leukemias after malignant lymphomas (*13*) and solid tumors after cancer of the cervix uteri (*3*). Furthermore, the present investigation included only cases of second primary cancers of organs other than those of the first cancer, whereas the Connecticut study included multicentric tumors within the same organ or in paired organs as second cancers. If the observed and expected second cancers occurring in the same organ are disregarded, the RR is only reduced from 1.31 to 1.23 in Connecticut.

Differences also exist between Denmark and Connecticut in medical surveillance of cancer patients and different attitudes by the physicians and the Registries in accepting a new tumor as an independent primary cancer. These known and presumed differences may lead to an overestimate of the risk of second primary cancer development in Connecticut if metastatic lesions were classified incorrectly as new primaries, whereas the risk of second primary

TEXT-TABLE 2.—*Distribution of persons with simultaneous primary cancers among males and females, Denmark, 1943–80*[a, b]

Cancer site/type	Cancer site																																		
	Lip	Tongue	Salivary	Oral	Pharynx	Esophagus	Stomach	Sm intest	Colon	Rectum	Liver	Pancreas	Nasal	Larynx	Lung	Breast	Cervix	Corpus	Uterus, NOS	Ovary	Prostate	Testis	Kidney	Bladder	Melanoma	Eye	Brain	Thyroid	Bone	Connective	NHL	HD	Myeloma	Leukemia	Other
Lip	0																																		
Tongue	1	0																																	
Salivary	1	2	0																																
Oral	0	3	2	1																															
Pharynx	0	1	0	2	0																														
Esophagus	1	0	1	0	5	0																													
Stomach	3	0	1	1	4	16	0																												
Sm intest	0	0	0	0	0	0	6	0																											
Colon	3	1	1	2	1	7	69	8	57																										
Rectum	2	0	1	1	1	10	56	3	94	0																									
Liver	0	0	2	0	1	2	15	2	16	14	4																								
Pancreas	0	0	1	0	0	4	16	0	21	12	28	1																							
Nasal	0	0	0	1	1	0	0	0	1	1	0	0	0																						
Larynx	2	0	0	1	4	2	4	0	0	1	1	2	0	0																					
Lung	10	0	2	1	2	10	38	6	37	49	20	22	1	17	8																				
Breast	3	3	4	1	1	2	37	2	52	30	11	7	2	0	24	1																			
Cervix	0	0	0	0	2	2	12	0	13	16	2	2	0	0	11	58	1																		
Corpus	0	1	0	0	0	0	3	1	16	4	3	0	0	0	6	53	16	3																	
Uterus, NOS	0	0	0	0	0	0	2	0	1	1	0	0	0	0	0	2	0	2	0																
Ovary	0	0	0	0	0	0	26	0	76	26	3	8	0	0	7	41	14	78	3	3															
Prostate	4	0	1	0	1	6	56	2	39	37	7	21	0	1	56	0	0	0	2	0	0														
Testis	0	0	0	1	1	0	0	0	1	1	0	0	0	0	4	0	0	0	0	0	0	1													
Kidney	1	0	0	0	1	7	39	3	45	36	26	29	1	0	70	12	11	5	1	7	34	2	26												
Bladder	0	0	1	2	0	3	29	0	32	37	7	12	1	1	55	26	13	5	1	9	173	2	104	1											
Melanoma	1	0	1	1	0	0	2	0	3	3	0	0	0	1	2	9	2	2	0	2	3	0	1	3	0										
Eye	0	0	0	0	0	0	3	0	1	5	0	2	0	0	2	4	0	0	1	0	0	0	1	0	1	0									
Brain	0	0	1	0	1	1	6	0	6	4	2	2	0	0	25	4	3	2	0	4	4	1	22	2	1	0	9								
Thyroid	1	0	0	0	0	0	2	0	2	1	2	0	0	0	3	6	0	2	0	1	4	0	6	5	2	0	0	0							
Bone	0	0	0	0	0	0	2	0	0	1	0	0	0	1	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0						
Connective	0	0	0	0	0	2	0	0	1	0	0	1	0	0	1	4	1	2	0	0	2	0	1	3	0	0	0	1	0	0					
NHL	0	0	0	0	0	1	7	0	4	9	0	3	1	0	12	9	4	1	0	2	12	0	5	4	2	0	4	4	0	0	0				
HD	0	0	0	0	0	0	3	0	2	2	0	2	0	0	7	3	3	0	0	0	2	1	5	7	0	0	1	0	0	1	1	0			
Myeloma	0	0	0	0	0	0	7	0	3	0	1	2	0	0	8	9	0	1	0	0	4	0	13	0	1	0	0	0	0	0	1	0	1		
Leukemia	2	0	1	3	1	5	30	1	2	21	9	5	3	5	36	12	3	2	0	5	18	3	18	15	3	0	6	1	1	0	5	4	1	2	
Other	2	1	2	2	3	6	17	6	5	13	4	6	0	2	18	25	10	10	0	17	12	0	21	23	2	2	10	8	1	0	6	5	1	13	12
Total[c]	37	13	25	25	33	93	512	40	622	492	182	209	13	45	572	458	200	218	16	332	501	18	553	576	48	22	121	46	10	20	97	49	53	236	260

[a] Abbreviations: Oral = oral cavity, Sm intest = small intestine, Nasal = nasal cavities, Corpus = uterine corpus, Connective = connective tissue, NHL = non-Hodgkin's lymphoma, HD = Hodgkin's disease, Myeloma = multiple myeloma, Other = other cancers and unknown primary sites.

[b] A total of 3,439 persons developed 6,878 simultaneous cancers. There were 131 persons who developed simultaneous cancers of the same site. *Numbers in the interior* represent patients with pairs of simultaneous cancers.

[c] Each number in the total row represents the sum of the vertical and horizontal tabulations for that particular cancer site, with the intersection counted once. For example, in the fourth column, 25 is the number of persons who developed a simultaneous tumor of the oral cavity; however, the total number of simultaneous cancers of the oral cavity is 26 because 1 person (the intersection of oral cavity row with oral cavity column) developed a simultaneous tumor of this same site.

cancers in Denmark may be underestimated because of conservative coding and reporting practices.

For both sexes combined, the site-specific RR in our study (table 1C) was significantly increased for second cancers of the pharynx (1.4), small intestine (1.7), lung (1.1), kidney (1.4), urinary bladder (1.3), bone (1.6), and connective tissue (1.5), and for ANLL (1.5). The highest RR of ANLL was seen within the 1- to 4-year interval of follow-up (2.0; 95% CI = 1.6–2.5). Any ANLL appearing early after the first primary cancer diagnosis may be treatment induced. The risk of ANLL was still elevated 10–19 years after initial cancer diagnosis, and treatment of recurrent first primary cancers could be associated with these late appearances. Among the sex-specific initial cancers (tables 1D, 1E), only the RR of second testis cancer (1.9) and uterus, NOS (1.4), were elevated.

Decreased second cancer risk in both sexes combined was observed for cancers of the esophagus (RR = 0.9), stomach (0.7), rectum (0.8), liver and gallbladder (0.9), and for multiple myeloma (0.6), as well as decreased RR for cancers of the breast (0.6), cervix (0.6), corpus uteri (0.9), and prostate (0.8). These decreased RR may be explained by the registration and notification practices in Denmark, which tend to prevent registration and acceptance of an additional cancer at the same or adjacent site. Reduced medical surveillance for elderly cancer patients may also play a role as indicated by the deficit of multiple myeloma and prostate cancer.

Age at First Primary Cancer

The pattern of second cancer development was considered separately for 4 intervals of age at first cancer diagnosis. Childhood cancers and cancers of adolescence (ages 0–19 yr) comprised 1.5% of all tumors and were predominantly leukemias, lymphomas, sarcomas, and cancers of the brain, kidney, and eye. Cancer in young adults (aged 20–39 yr) comprised 6.9% of all cases. Cancer in middle-aged adults, including the women in the menopausal period (aged 40–59 yr), comprised 32% of all cases, and cancer in patients 60 years of age and older comprised 59.8% of all cancers. Risks of second cancers by age at first diagnosis are presented in figure 1.

A significant overall elevated risk of second cancer development was present in all age groups below 60 years, except for females 0–19 years of age at diagnosis (both sexes: under 19, RR = 2.4; ages 20–39, RR = 1.3; ages 40–59, RR = 1.1). In contrast, a statistically significant deficit of second cancer in persons aged 60 years or more at diagnosis (RR = 0.8) might be due to reduced surveillance for elderly cancer patients that would lead to underdiagnosis of multiple primary cancers.

For all age groups under 60 years at primary cancer diagnosis, the risk of a second cancer was higher among men than among women. For persons below the age of 40 at the first diagnosis, this sex difference persisted for 30 years. The RR for women may be underestimated because we could not adjust the expected numbers for cancers occurring within the same site as the index site, which are not registered by the Registry. However, this would also be true for second cancers in men. The small difference in the risk of second tumors between men and women might thus be associated with the propensity for cancers of smoking-related sites to occur frequently in the same individual, given that men smoke more than women. The finding of a twofold to fourfold increased RR of second cancer after 20 years of follow-up among patients under age 20 is consistent with findings of another investigation (*23*), although the RR in our study is approximately one-half that found previously.

A consistent observation for all age intervals was the elevated risk of subsequent cancers of the bone and connective tissue. Among the patients under age 20, second cancers of the brain (RR = 5.2; *n* = 7) and liver (RR =

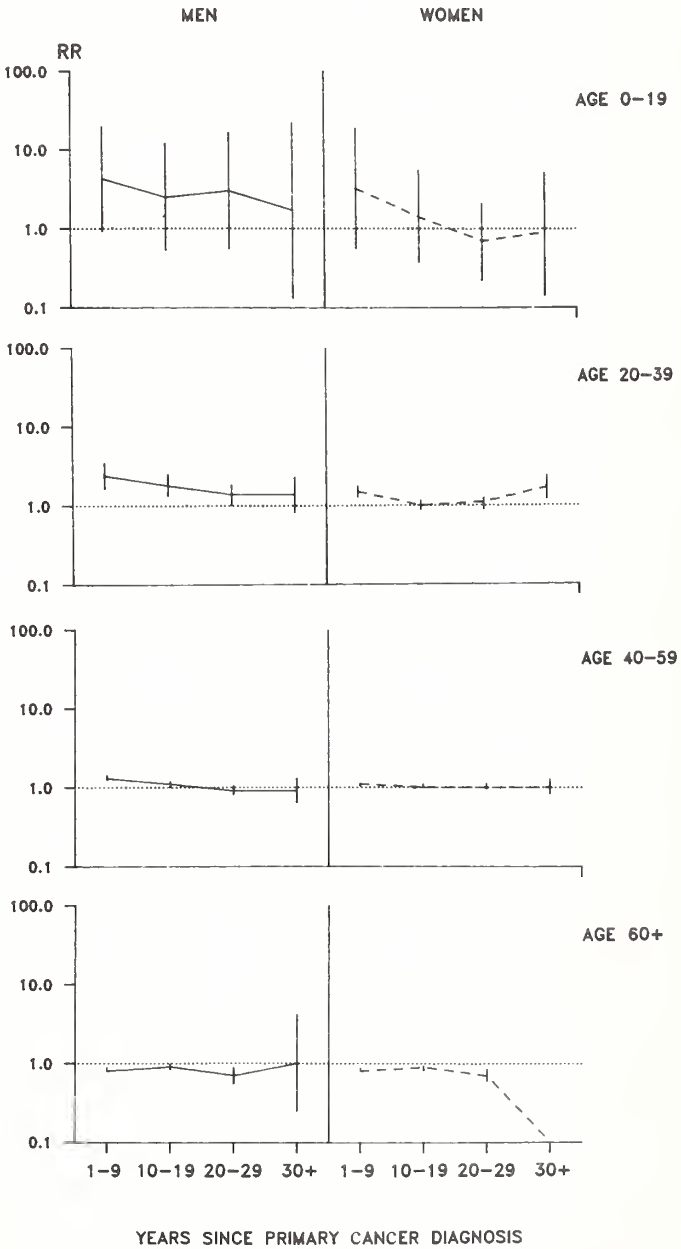

FIGURE 1.—The RR and 95% CI of second primary cancers by age at first cancer diagnosis for all cancer sites among males and females in Denmark, 1943–80.

33; $n = 2$), and ANLL (RR = 6.3; $n = 3$) were observed in excess. It has been suggested that genetic predisposition is important for cancers developing in this young age group (*4*), and this may offer an explanation for the excess of brain tumors (*24*) and possibly osteosarcomas. The role of treatment and the possible combination of environmental and genetic factors for subsequent cancer development cannot be distinguished in the present study.

Relationships Between Sites of First and Second Primary Cancers

The overall risk of a new primary cancer among all cancer patients is composed of excesses and deficits of various second tumors after different first primary cancers (*3–13*). Thus the constellation of multiple tumors that occur in individuals with the same first primary cancer may provide informative clues to factors that influence risk. For example, smoking habits are likely to contribute to the associations found between tumors of the respiratory and upper digestive tract above the diaphragm, the urinary system, the pancreas, and the cervix uteri. Nutritional and hormonal factors probably affect the associations observed between cancers of the large bowel, breast, and female genital organs. To investigate the possible influence of anticancer therapy on subsequent tumor development, we examined risks in long-term survivors who frequently received radiotherapy or chemotherapy. Finally, a number of associations emerged for which no explanations are readily available.

Smoking-related Cancers of Buccal Cavity, Upper Respiratory-Digestive Tracts, and Urinary Tract

Tobbaco smoking is related to cancers of the larynx, lung, lip, tongue, gum and mouth, pharynx, esophagus, bladder and ureter, and renal pelvis (*25*). Cancer of the pancreas may also be associated with smoking (*26*), and recent observations suggest that smoking increases the risk of cancer of the liver (*27*), adenocarcinoma of the kidney (*28*), cancer of the cervix uteri (*29*), and cancer of the nasal passages (*30*).

Text-table 3 shows the reciprocal risk elevations for cancers of the buccal cavity and pharynx, esophagus, pancreas, and respiratory and urinary tracts. Patients with cancers of the mouth, tongue, and pharynx generally had two to five times higher RR of developing a new cancer of organs in close proximity to the initial primary. The highest RR were seen for cancer of the tongue (20.8) following mouth cancer and vice versa (12.0). Cancers of the esophagus also developed two to five times more frequently than expected in persons with tongue, mouth, and pharyngeal tumors as did laryngeal cancer following tongue and pharyngeal tumors. Cancer of the lip was unrelated to tumors of smoking-related sites outside the oral cavity.

Lung cancer patients had a significant threefold increased RR of laryngeal cancer, and laryngeal cancer was followed by a similar elevated risk of lung cancer. Lung cancer patients had nonsignificant RR of 1.2 to 1.8 of developing cancers of the tongue, mouth, pharynx, and esophagus, whereas the RR of developing lung cancer following cancers of the oral cavity and pharynx was approxi-

TEXT-TABLE 3.—*Reciprocal associations (RR) between smoking-related cancer sites among males and females in Denmark, 1943–80*[a]

	Lip		Tongue		Mouth		Pharynx		Esophagus		Larynx		Lung		Kidney		Bladder	
Tongue	0.0	1.8^b																
Mouth	6.3^b	2.4^b	20.8^b	12.0^b														
Pharynx	1.4	0.9	0.0	4.8	4.2	2.6												
Esophagus	1.3	1.0	6.3	3.4	0.0	5.3^b	4.0	2.5										
Larynx	1.9	0.1^b	1.6	4.5	2.4	1.1	2.3	5.1^b	0.2	0.0								
Lung	0.7	1.0	1.8	2.5^b	1.8	2.4^b	1.2	1.9^b	1.3	0.8	3.1^b	2.6^b						
Kidney	0.3	0.8	0.0	3.0	0.0	0.3	1.6	1.7	0.3	2.6	0.3	0.5	0.89	2.7^b				
Bladder	0.9	0.9	1.1	2.2	1.1	1.3	1.5	0.8	0.6	0.8	1.5	1.4	1.6^b	1.6^b	3.2^b	7.1^b		
Pancreas	0.0	0.7	0.0	1.4	0.0	0.5	3.2	1.0	0.0	0.8	1.4	1.7^b	0.5	1.4	2.7^b	1.3	1.4	1.0

[a] For example, in the first row of the table, 0.0 is the RR of lip cancer after cancer of the tongue and 1.8 is the RR of tongue cancer following an initial cancer of the lip.

[b] $P < .05$.

mately twofold. Lung cancer patients also had elevated risks of developing cancer of the urinary bladder (RR = 1.6), kidney (2.7), and pancreas (1.4). The RR of lung cancer was increased in patients with bladder cancer (1.6) but not with kidney cancer (0.9). The lung, bladder, and kidney associations were significant in men only, although comparable risks were seen for women. The relationship was clear between bladder and kidney cancers (including the ureter and renal pelvis), with an RR of 3.2 for kidney tumors following bladder cancer and an RR of 7.1 for bladder tumors following kidney cancer. Cancer of the pancreas was significantly elevated following cancer of the larynx (RR = 1.7), with nonsignificant excesses seen after cancers of the tongue (RR = 1.4) and kidney (RR = 1.3).

Cancer of the cervix uteri was increased in women with initial cancers of smoking-related sites such as the oral cavity and pharynx, esophagus, pancreas, larynx, lung, kidney, and bladder. Women with cervical cancer also had a higher risk of developing cancers of these sites (text-table 4). However, the RR for second cancer of the cervix was significantly increased (1.7) only when women with an initial cancer of a smoking-related site were combined.

When bidirectional associations appear to be independent of intervals between tumor diagnoses, common etiologic factors are suspected. Tobacco smoking appears to underlie the associations between cancers of the oral cavity and pharynx, esophagus, respiratory system, and urinary tract. Not only do smokers have an increased risk of developing cancer of these sites, but persons who develop one of these cancers have an increased risk of yet another smoking-related tumor. One-third of all 481 second tumors seen in lung cancer patients could be considered to be related to smoking, which explains the 20% excess of second primary cancer among lung cancer patients (*7*).

For cancers of the oral cavity and pharynx, the elevated RR of cancer of adjacent sites can be attributed to tobacco (and alcohol), and the same applies to the reciprocal associations between kidney and bladder cancers. However, it is difficult for us to rule out the influence of misdiagnosis and misclassification of metastatic spread on the risk estimates for tumors arising from the same organ system, and host factors may play an important role in promoting multifocal tumors and predisposing to environmental risk factors. The slightly increased RR of pancreatic cancer following cancers of the lung and larynx supports the evidence linking smoking to pancreatic cancer in other studies (*26, 31*).

Recent evidence suggests that smoking increases the risk of cancer of the cervix uteri (*29*), so it is noteworthy that the RR of cervical cancer was consistently increased following cancers of the smoking-related sites (text-table 4). However, the association may be confounded by socioeconomic and other characteristics associated both with smoking and cervical cancer (*32*).

TEXT-TABLE 4.—*Reciprocal associations (RR) between cancer of the cervix uteri and smoking-related cancers among females in Denmark, 1943–80*[a]

Tobacco-related cancer site	Cervix uteri Second site	 First site
Oral cavity and pharynx	1.2	1.4
Esophagus	3.2	2.0[b]
Pancreas	2.2	1.2
Larynx	3.0	2.1
Lung	1.7	2.8[b]
Kidney	1.7	1.4[b]
Bladder	1.4	3.0[b]
All sites	1.7[b] 1.2–2.2[c]	2.1[b] 1.9–2.3[c]

[a] For example, 1.2 is the RR of cancer of the cervix uteri developing after an initial cancer of the oral cavity and pharynx, and 1.4 is the RR of a cancer of the oral cavity or pharynx developing after an initial primary cancer of the cervix uteri.

[b] $P < .05$.

[c] Values are 95% CI.

TEXT-TABLE 5.—*Reciprocal associations (RR) between cancers of hormone dependent organs and the colon among females in Denmark, 1943–80*[a]

	Colon	Breast	Corpus uteri
Breast	0.9 1.1		
Corpus uteri	1.8[b] 1.5[b]	1.0 1.2[b]	
Ovary	2.6[b] 1.7[b]	1.3[b] 1.1	0.8[c] 2.3[b]

[a] For example, in the first row of the table, 1.1 is the RR of colon cancer developing after an initial primary cancer of the breast, and 0.9 is the RR of breast cancer developing after a colon cancer.

[b] $P < .05$.

[c] The RR = 2.7 when allowance is made for hysterectomies (and thus possibly oophorectomies) in calculation of risk.

Hormone- and Fat-related Cancers of the Breast, Female Genital Organs, and Digestive Organs

Text-table 5 shows the reciprocal RR of multiple primary cancers involving the breast, endometrium, ovary, and colon. Significant relationships were seen between endometrium–colon and ovary–colon cancers in both directions. The RR was not increased for colon cancer following breast cancer or for breast cancer following colon cancer. The relationship between cancers of the breast and the female reproductive organs was weak (RR = 1.0–1.3) and only significant in one direction. Cancer of the endometrium after ovarian cancer was seen twice as often as expected, whereas the RR was not increased in the reverse direction. However, when we reduced the population-at-risk for uterine and ovarian cancers by subtracting women who had a hysterectomy (and thus probably an oophorectomy), a significant RR of 2.7 of ovarian cancer after endometrial cancer was uncovered (*9*).

The RR of cancers of the colon (1.3), pancreas (2.0), and corpus uteri (2.0) were increased, although not significantly, following cancer of the liver and biliary tract, whereas cancer of the ovary (3.2) was significantly elevated. The RR of pancreatic, endometrial, and ovarian cancers were elevated particularly within the first 5 years of diagnosis of the initial cancer. Increased RR of endometrial (3.2) and ovarian cancers (3.1) were observed following cancer of the pancreas.

The associations seen between cancers of the digestive tract (colon, pancreas, liver, and biliary tract), breast, and female genital organs (endometrium, ovary) are not easily explained. The ovaries are frequent metastatic sites for breast and colon cancer and, with misdiagnosis of metastatic spread within the abdominal cavity, could bias the results. Differential diagnostic problems of a physician's determining the primary site of an abdominal tumor may also play a role. The excess risks of ovarian cancer following colon cancer and colon cancer following ovarian cancer were limited to the first 5 years of follow-up, and the excess of endometrial cancer following ovarian cancer was only seen during the first 9 years of follow-up.

Cancers of the colon, rectum, biliary tract, pancreas, breast, endometrium, ovary, and prostate may have similar dietary and nutritional determinants, such as fat intake (*33*). However, the biologic mechanisms involved are not clear, and the suggested relationship with fat for many of these sites is based mainly on evidence from international correlations (*34*). Some of these cancers are hormone dependent, particularly cancers of the breast, corpus uteri, and ovary, and the risk for females developing colon cancer may also be related to endocrine factors (*35*). Thus an association in both directions between cancer of the colon and cancers of the endometrium and ovary is interesting. The overall absence of strong bidirectional associations between cancers of these sites may be due to a weak association with fat (*2, 18, 19*), little variation in the diet of the Danish population, or a possible underreporting of multiple primary cancers.

Obesity has been associated with cancers of the endometrium and breast (*29*), possibly due to the increased production of endogenous estrogens (*36*). Several studies show an association between the use of estrogen unopposed by progesterone and endometrial cancer (*37*); and some evidence indicates that estrogens may cause breast tumors, particularly in high-risk individuals (*38*). Ovarian cancer has also been linked to estrogens (*39*). In our study, we (*9*) observed excesses of breast cancer following endometrial cancer, ovarian cancer after breast cancer, endometrial cancer following ovarian cancer, and an increased risk of ovarian cancer following endometrial cancer (text-table 5). These data are consistent with the hypothesis that hormonal factors, including endogenous estrogens, may influence tumor development for these cancer sites. The development of liver tumors (hepatocellular carcinomas) has been associated with the use of oral contraceptives (*40*).

Radiation- and Chemotherapy-associated Sites

Ionizing radiation (*41*) and certain chemotherapeutic drugs (*42*) used in the treatment of cancer are known carcinogens. In the past, notification of treatment to the Registry was deficient (*43*), and thus we were unable to group cancer patients according to treatment. However, it is likely that patients reported to the Registry as irradiated were indeed irradiated (*43*), although the converse is not necessarily true. To evaluate the possible influence of irradiation on second cancer development, we classified index cancer sites by the percentage reported as irradiated. However, it should be kept in mind that the observed RR of second primary cancers are conservative estimates due to the inclusion of a proportion of nonirradiated patients in the cohorts of patients with frequently irradiated index cancers. Because most radiation-induced cancers, except leukemia, occur 10 years or more after exposure, we examined the risks of several solid tumors in this period that developed after initial cancers for which at least 50% of the patients received radiation as part of their initial treatment (text-table 6). For comparison, RR are presented also for patients surviving 10 or more years after a cancer for which 4% of the patients on average received radiotherapy. This low-exposure group is dominated by patients with cancers of the colon and stomach. The risk of subsequent ANLL was also evaluated during the 1- to 9-year follow-up interval (text-table 7).

More than one-half of the patients with first cancers of the head and neck, genital organs, and breast, and malignant lymphoma were given radiotherapy as part of their initial treatment. A 2.7-fold and a 1.5-fold increased risk of thyroid and breast cancers, respectively, were observed following head and neck cancer. The thyroid gland is known to be sensitive to radiation, and increased cancer risks have previously been described following x rays to the head and neck region (*44*), treatment for tinea capitis (*45*), and among atomic bomb survivors (*46*). It is unlikely that the observed excess of thyroid cancer is a result of misdiagnosed metatases because the morphologic characteristics are distinct, and 95% of all thyroid cancers were histologically verified (*12*). Intense medical surveillance of the head and neck region could increase the number of observed thyroid cancers beyond that expected from general population rates.

The breast cancer excess is unlikely to be attributable to radiation of the head and neck region because in most instances the breast would not be in or near the therapeutic fields. Even if some radiation scatter might expose the breast, the dose would be of such low magnitude that radiogenic breast tumors would be rare events. A bidirectional association between salivary gland tumors and breast cancer has been described (*47, 48*), but this was only suggested among long-term survivors in our study (*5, 8*).

The RR of cancers of the colon (1.2), rectum (1.5), bladder (2.6), and connective tissue (2.5) was increased in long-term survivors with a first cancer of genital organs for which radiotherapy is given frequently. All these organs are close to the radiation fields used to treat genital cancers (*49*), although some differences do occur between the field configurations for male and female genital cancer treatments. The RR for colon and rectal cancer are compatible with those seen for other irradiated populations, e.g., patients with ankylosing spondylitis and metropathia hemorrhagica (*50, 51*). However, for cancers of the colon and rectum, similar RR are also seen among long-term survivors with cancer of infrequently irradiated sites. The sites comprising this low-exposure group are predomi-

TEXT-TABLE 6.—*Significantly elevated RR of solid tumors in long-term survivors (10+ yr) with initial cancers for whom 50% or more were treated with radiation and for long-term survivors with initial cancers infrequently treated with radiation among males and females in Denmark, 1943–80*

Frequently irradiated		Second primary site	Frequently irradiated		Infrequently irradiated sites[a]	
Site/type	Percent given radiotherapy		RR	95% CI	RR	95% CI
Head and neck[b]	76	Thyroid	2.7	1.0–6.0	0.8	0.1–2.8
		Female breast	1.6	1.0–2.2	1.0	0.8–1.4
Genital organs[c]	65	Colon	1.2	1.0–1.4	1.0	0.8–1.3
		Rectum	1.5	1.2–1.8	1.4	1.1–1.9
		Bladder[d]	2.6	2.2–3.2	0.8	0.5–1.2
		Connective tissue	2.5	1.2–4.6	0.7	0.0–3.8
Female breast	69	Salivary gland	3.2	1.3–6.5	0.8	0.0–4.7
		Esophagus	1.7	1.0–2.9	1.0	0.4–2.1
		Lung	1.7	1.3–2.1	1.0	0.7–1.3
		Ovary	1.5	1.2–1.9	0.5	0.2–1.1
		Connective tissue	4.2	2.1–7.6	0.7	0.0–3.8
Hodgkin's disease and NHL	64	Lung	1.8	1.0–2.9	1.0	0.7–1.3
		Female breast	2.1	1.1–3.5	1.0	0.8–1.4
		Bladder[d]	2.6	1.3–4.7	0.8	0.5–1.2

[a] Sites for which less than 10% of patients received radiotherapy include cancers of the stomach, small intestine, colon, liver and gallbladder, and pancreas; on average, 4% received radiotherapy.

[b] Head and neck cancers include cancers of the lip, tongue, salivary gland, gum and mouth, pharynx, larynx, and nasal cavities.

[c] Included in cancers of the genital organs are cancers of the testis, cervix uteri, and corpus uteri.

[d] Bladder cancer includes papillomas.

nantly within the abdomen, and common risk factors for gastrointestinal cancers or misdiagnosed metastases may account for some of the increased risks.

A large proportion of all breast cancer patients received radiotherapy (text-table 6). The increased risks of cancers of the esophagus and lung following breast cancer are consistent with a radiation effect which has been seen in studies of atomic bomb survivors (*52*). It is unlikely that the increased risk of ovarian cancer following breast cancer is related to castration radiotherapy because only 6% of Danish breast cancer patients received such treatment (*53*). The elevated risk of cancer of the salivary glands is probably not due to radiation because the distance from the usual radiation treatment fields would be great. A more probable explanation may be that these cancer sites share some common etiology.

Cancers of connective tissue (RR = 2.5; 95% CI = 1.6–3.9), and bone (RR = 2.4; 95% CI = 1.2–4.4) were in excess when observations from all the frequently irradiated sites were combined. A further evaluation that included consideration of the configuration of the radiation fields and actual sarcoma site would be necessary before radiation could be implicated.

Solid tumors were also in excess among long-term survivors with malignant lymphoma, in particular cancers of the lung, female breast, and bladder (text-table 6). Radiation may have increased the risk of second cancers in some instances, such as following the inverted Y-irradiation for Hodgkin's disease that exposes a large proportion of the body trunk. Common etiologies and misdiagnoses of lymphatic infiltrations could also be involved.

The RR of ANLL occurring 1–9 and 10 or more years after initial cancers which are frequently treated with radiation are shown in text-table 7. Significantly increased RR were noted during the first period among patients with initial cancers of the genital organs (1.9), female breast cancer (2.7), and malignant lymphoma (Hodgkin's disease, 20.6; NHL, 3.5). Interestingly, the RR of ANLL remained significantly elevated among long-term survivors of breast cancer (2.3) and malignant lymphoma (Hodgkin's disease, 14.3; NHL, 7.1).

The induction of acute leukemia, especially ANLL, is a well-known consequence of radiation (*54–56*), and the pattern of increased risk of ANLL is different from that

TEXT-TABLE 7.—*The RR of ANLL following initial cancer sites frequently treated with radiation (≥50%) among males and females in Denmark, 1943–80*

First primary cancer site/type	Percent given radiotherapy	Yr after first primary cancer			
		1–9		10+	
		RR	95% CI	RR	95% CI
Head and neck[a]	76	1.1	0.4– 2.5	0.7	0.1– 2.1
Genital organs[b]	65	1.9	1.1– 3.1	0.5	0.2– 1.1
Female breast	69	2.7	1.9– 3.9	2.3	1.3– 3.7
Hodgkin's disease and NHL	64	8.4	4.0–15.5	8.9	2.9–21.0
Infrequently irradiated sites[c]	<10	1.2	0.6– 2.2	0.3	0.0 –1.4

[a] Head and neck cancers include cancers of the lip, tongue, salivary gland, gum and mouth, pharynx, larynx, and nasal cavities.

[b] Included in cancers of the genital organs are cancers of the testis, cervix uteri, and corpus uteri.

[c] Cancer sites for which less than 10% of patients received radiotherapy include stomach, small intestine, colon, liver and gallbladder, and pancreas; on average, 4% of patients received radiotherapy.

observed for solid tumors which usually occur 10 or more years after radiotherapy. The appearance of excess ANLL within the first 1–9 years of follow-up in the present investigation (text-table 7) is consistent with previous reports of the pattern of excess risk over time (*57*). The excess noted in patients surviving 10 years or more may be related to treatment of recurrent disease. For Hodgkin's disease and NHL, chemotherapy undoubtedly contributed to the increased risk of leukemia as reported by previous investigators (*54, 58–60*). Our present findings do not allow us to state whether radiation, chemotherapy, or both, are associated with ANLL; but previous studies have indicated that alkylating agents are much more likely to be responsible for the increased leukemia risk than is radiotherapy (*61*).

Other Associations Between Sites

Associations observed between first and second cancer sites other than those presented in previous tables are summarized in text-table 8. Reciprocal and significantly increased RR were observed for NHL after leukemia (2.6) and vice versa (2.1). The bidirectional relationship was strong between bone and eye tumors, but the numbers involved were small, and only the RR of eye tumors following bone cancer was significant (20.0; *n* = 3). Thyroid cancer was followed by an increased RR of NHL (4.4), whereas the excess risk for thyroid cancer (3.1) following NHL was nonsignificant. Brain tumors were followed by an increased RR of kidney cancer (3.2) and bone tumors. (6.9); nonsignificant elevations (RR of 1.6 and 1.9, respectively) were observed in the opposite direction.

The importance of these associations is uncertain because so many comparisons were performed that chance alone could be a factor; some observations have possible explanations. Most physicians find CLL difficult to distinguish from low-grade, small-cell lymphocytic lymphoma which frequently has circulating cells (*62*). Genetic predisposition may explain the association between cancers of the eye and bone, especially for childhood tumors involving retinoblastoma followed by osteosarcoma (*63*). Whether the bidirectional associations between thyroid cancer and NHL are due to radiation given to the head and neck region, metastatic spread, misdiagnosis, close medical supervision, or some combination of these factors has not been explained.

Significant unidirectional increases in RR were seen for kidney cancer (including the ureter and renal pelvis) following cancers of the ovary (2.1), bone (3.5), and leukemia (2.9). The number of liver and biliary tract cancers was higher than expected after cancers of the lung (RR = 1.9) and small intestine (RR = 5.7). Following cancer of the small intestine, the RR was increased only during the first 5 years (11.1); following lung cancer, the RR increased with time since diagnosis to 2.9 among patients surviving 10 or more years (95% CI = 0.9–6.7).

Brain tumors were followed by increases in the RR of melanoma of the skin (2.5) and tumors of connective tissue (4.9). Although the highest RR were seen in long-term survivors, no clear pattern with time since diagnosis of the first tumor emerged. Patients with tumors of the connective tissue had an increased RR of NHL (2.9), and most of the excess was seen among long-term survivors and was statistically significant (4.2; 95% CI = 1.1–10.7).

TEXT-TABLE 8.—*Reciprocal associations (RR) between cancers of selected sites with significant RR in at least one direction, among males and females in Denmark, 1943–80*

First primary site/type	Second primary site/type	RR	95% CI	First primary site/type	Second primary site/type	RR	95% CI
Stomach	Ovary	1.9	1.2– 2.9	Ovary	Stomach	0.9	0.5– 1.3
Small intestine	Livery, biliary	5.7	1.5–14.6	Liver, biliary	Small intestine	—[a]	—
Lung	Livery, biliary	1.9	1.2– 2.9	Liver, biliary	Lung	0.8	0.2– 2.1
Female breast	Melanoma	1.4	1.0– 1.8	Melanoma	Female breast	1.1	0.8– 1.4
Ovary	Kidney	2.1	1.3– 3.2	Kidney	Ovary	0.0	—
Ovary	Bladder	2.2	1.4– 3.3	Bladder	Ovary	0.8	0.4– 1.4
Ovary	Leukemias	1.9	1.0– 3.1	Leukemias	Ovary	0.2	0.0– 1.3
Bladder	Prostate gland	1.3	1.1– 1.5	Prostate gland	Bladder	1.0	0.8– 1.2
Brain	Kidney	3.2	2.1– 4.7	Kidney	Brain	1.6	0.7– 3.0
Brain	Melanoma	2.5	1.2– 4.5	Melanoma	Brain	1.2	0.5– 2.3
Brain	Bone	6.9	1.9–17.7	Bone	Brain	1.9	0.2– 6.8
Brain	Connective tissue	4.9	1.6–11.3	Connective tissue	Bone	0.0	—
Thyroid gland	NHL	4.4	1.6– 9.7	NHL	Thyroid gland	3.1	0.6– 9.1
Bone	Kidney	3.5	1.1– 8.2	Kidney	Bone	0.0	—
Bone	Eye	20.0	4.0–58.4	Eye	Bone	4.3	0.1–24.2
Connective tissue	NHL	2.9	1.1– 6.4	NHL	Connective tissue	0.0	—
Multiple myeloma	Kidney	2.9	1.3– 5.8	Kidney	Multiple myeloma	1.1	0.3– 2.8
Multiple myeloma	Brain	3.4	1.1– 7.8	Brain	Multiple myeloma	0.7	0.1– 2.4
Multiple myeloma	ANLL	9.1	3.3–19.8	ANLL	Multiple myeloma	—[b]	—
Leukemias	Lip	3.1	1.2– 6.3	Lip	Leukemias	0.9	0.5– 1.4
Leukemias	Kidney	2.9	1.7– 4.5	Kidney	Leukemias	1.3	0.6– 2.3
Leukemias	NHL	2.6	1.2– 5.0	NHL	Leukemias	2.1	1.1– 3.7

[a] Small intestine was not included as a second cancer in the analysis.

[b] We did not include ANLL as a first primary cancer in the analysis.

The unidirectional associations in text-table 8 may be due partially to metastatic spread of the primary cancer being misclassified as a new tumor. This may have occurred for ovarian cancer following stomach cancer (RR = 1.9), the so-called Krukenberg tumor. The close anatomical location between the bladder and prostate makes direct spread of bladder cancer to the prostate a possibility (*11*), and increased medical surveillance would lead to an overestimate of the RR for prostate cancer (1.3). Cancers of the brain (RR = 3.4) and kidney (RR = 2.9) following multiple myeloma may be due to misinterpreted tumor infiltrates or closer medical attention because multiple myeloma frequently is diagnosed within the skull and kidney (*64*). The reason for the excess of kidney cancer following cancers of the bone (RR = 3.5) and brain (RR = 3.2) is not entirely clear but may be due to the slightly increased autopsy rate among cancer patients.

An increased risk of ANLL was observed following multiple myeloma, and all 6 ANLL cases were seen during the first 5 years of follow-up (RR = 11.8; 95% CI = 4.3–25.6). Leukemia was also in excess following ovarian cancer, particularly 1–4 years (RR = 2.8) and 5–9 years (RR = 1.9) after diagnosis. Excess leukemia following multiple myeloma and cancer of the ovary was previously reported to be related to chemotherapy (*65, 66*).

Tumors of the urinary bladder (RR = 2.2) were also in excess following cancer of the ovary. An increasing trend with time and a significant RR of 3.9 (95% CI = 2.2–6.4) were observed for bladder tumors among long-term survivors. Whether this association is due to chemotherapeutic drugs or perhaps to closer medical supervision including cystoscopy among patients with a gynecologic cancer should be examined further.

CONCLUSION

The present study indicates the usefulness of a population-based cancer registry in evaluation and quantification of the risk of second primary cancers. The long period of follow-up available for the Danish Registry allows consideration of time trends in risk even for rare cancers. The overall risk of a person developing a second cancer at a different site from the first, RR = 0.99, as shown in this study may be underestimated, although an RR above 1.3 may be ruled out when possible underreporting is taken into account (*3*). Our results suggest that cancer patients overall are not at high risk of developing new malignant tumors, although elevated rates may occur for particular combinations of sites, especially those related to common risk factors. Conversely, the occurrence of one cancer does not appear to protect against the development of a new tumor in another organ.

No specific risk factor could be examined in the present descriptive study, but several etiologic leads have been suggested. Site-specific reciprocal associations indicate that the development of multiple primary cancers appear determined by shared risk factors, and cigarette smoking and hormonal factors are logical explanations for several constellations of tumors. In many instances, radiation and chemotherapy appear to increase the risk of second primary cancer.

Studies of multiple primary neoplasms provide researchers with a strategy to investigate the exogenous and endogenous determinants of cancer. To increase the value of the survey data, staffs of population-based cancer registries must give attention to improvements in registration of multiple cancers in the same individual. This is important with a view to future etiologic studies and to the identification of high-risk cancer patients who should be monitored closely for the early detection and management of second primary cancers.

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ALL CANCER SITES
BOTH SEXES

TABLE 1A.—*Characteristics of persons reported to the Danish Cancer Registry with any first primary cancer, 1943–80*[a]

Category	Male	Female	Total
No. with first primary cancer[b]	171,749	208,192	379,941
No. who developed a second primary cancer	6,370	8,714	15,084
Average age at diagnosis of first cancer, yr	63	60	61
Average yr of diagnosis of first cancer	1966	1965	1965
Person-yr of follow-up	586,365	1,120,371	1,706,736
Average follow-up, yr	3.8	5.6	5.0
Percent given radiotherapy for first cancer	26	44	36

[a] ICD-7 codes = 140–204.

[b] Number excludes all persons who survived less than 2 mo after the diagnosis of their first primary cancer or who developed a simultaneous cancer during this period. First primary cancers diagnosed only at autopsy or by death certificate are also excluded as are in situ cancers.

TABLE 1B.—*Microscopic confirmation among persons who developed second primary cancers after any first primary cancer in Denmark, 1943–80*

Microscopically confirmed	No.	Percent[a]
Both first and second cancers	11,981	79.4
Only the first cancer	1,864	12.4
Only the second cancer	911	6.0
Neither first nor second cancer	329	2.2
Total second primary cancers	15,085	100.0

[a] Minor discrepancies between table entries and row and column sums in this and subsequent tables are due to rounding.

ALL CANCER SITES
BOTH SEXES

TABLE 1C.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males and females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	379,941			229,154			102,664			56,430			379,941		
Person-yr in interval	292,653			586,770			379,625			447,688			1,706,736		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**1,879**	**2,742**	**0.7**[b]	**4,952**	**5,383**	**0.9**[b]	**3,447**	**3,597**	**1.0**	**4,806**	**4,859**	**1.0**	**15,084**	**16,580**	**0.9**[b]
Buccal cavity, pharynx	**37**	**63**	**0.6**[b]	**126**	**116**	**1.1**	**92**	**73**	**1.3**[b]	**100**	**90**	**1.1**	**355**	**341**	**1.0**
Lip	14	28	0.5[b]	48	48	1.0	33	29	1.2	26	32	0.8	121	136	0.9
Tongue	3	6	0.5	10	12	0.8	16	8	2.0[b]	10	11	1.0	39	37	1.1
Salivary gland	7	8	0.9	12	15	0.8	5	10	0.5	17	12	1.5	41	44	0.9
Gum, other mouth	4	11	0.4[b]	30	21	1.4	19	14	1.3	25	21	1.2	78	68	1.1
Pharynx	9	10	0.9	26	19	1.4	19	12	1.6	22	15	1.5	76	56	1.4[b]
Digestive system	**607**	**989**	**0.6**[b]	**1,556**	**1,872**	**0.8**[b]	**1,128**	**1,234**	**0.9**[b]	**1,688**	**1,673**	**1.0**	**4,979**	**5,768**	**0.9**[b]
Esophagus	20	37	0.5[b]	51	67	0.8	35	42	0.8	63	53	1.2	169	198	0.9[b]
Stomach	156	292	0.5[b]	379	520	0.7[b]	244	325	0.7[b]	333	389	0.9[b]	1,112	1,526	0.7[b]
Colon	153	259	0.6[b]	494	513	1.0	406	353	1.2[b]	563	519	1.1	1,616	1,645	1.0
Rectum	94	200	0.5[b]	296	377	0.8[b]	181	245	0.7[b]	338	321	1.1	909	1,143	0.8[b]
Liver, biliary	59	66	0.9	116	133	0.9	87	94	0.9	130	144	0.9	392	436	0.9[b]
Pancreas	99	98	1.0	142	195	0.7[b]	137	133	1.0	214	194	1.1	592	620	1.0
Respiratory system	**211**	**351**	**0.6**[b]	**725**	**661**	**1.1**[b]	**557**	**417**	**1.3**[b]	**663**	**531**	**1.2**[b]	**2,156**	**1,959**	**1.1**[b]
Nasal cavities, sinuses	4	6	0.7	11	11	1.0	4	7	0.6	14	9	1.6	33	33	1.0
Larynx	19	22	0.9	49	41	1.2	29	25	1.2	38	30	1.3	135	118	1.1
Trachea, bronchus, lung	180	304	0.6[b]	642	574	1.1[b]	502	362	1.4[b]	584	464	1.3[b]	1,908	1,704	1.1[b]
Breast	130	278	0.5[b]	385	618	0.6[b]	308	453	0.7[b]	471	673	0.7[b]	1,294	2,021	0.6[b]
Female genital tract	**228**	**257**	**0.9**	**556**	**579**	**1.0**	**347**	**420**	**0.8**[b]	**494**	**583**	**0.8**[b]	**1,625**	**1,838**	**0.9**[b]
Cervix uteri	50	91	0.6[b]	145	205	0.7[b]	84	142	0.6[b]	100	169	0.6[b]	379	606	0.6[b]
Corpus uteri	54	71	0.8[b]	148	161	0.9	114	120	0.9	156	180	0.9	472	532	0.9[b]
Uterus, NOS	11	6	1.9	22	11	1.9[b]	11	8	1.4	4	10	0.4[b]	48	35	1.4[b]
Ovary, fallopian tubes	106	75	1.4[b]	210	168	1.2[b]	106	125	0.9	165	184	0.9	587	551	1.1
Prostate gland	126	203	0.6[b]	260	365	0.7[b]	191	222	0.9[b]	214	252	0.8[b]	791	1,042	0.8[b]
Testis	4	5	0.7	18	10	1.8[b]	14	6	2.4[b]	15	6	2.5[b]	51	27	1.9[b]
Kidney, renal pelvis, ureter	137	79	1.7[b]	235	156	1.5[b]	128	105	1.2[b]	175	145	1.2[b]	675	485	1.4[b]
Bladder, other urinary	163	151	1.1	405	287	1.4[b]	249	185	1.3[b]	344	244	1.4[b]	1,161	867	1.3[b]
Melanoma of the skin	22	29	0.7	78	62	1.3	45	44	1.0	76	62	1.2	221	197	1.1
Eye	7	8	0.9	17	16	1.1	11	10	1.1	13	13	1.0	48	47	1.0
Brain, central nervous system	38	48	0.8	90	98	0.9	55	66	0.8	84	88	1.0	267	300	0.9
Thyroid gland	16	13	1.3	26	26	1.0	20	18	1.1	33	27	1.2	95	84	1.1
Bone	3	5	0.6	7	9	0.8	16	6	2.7[b]	17	7	2.3[b]	43	28	1.6[b]
Connective tissue	7	9	0.7	27	18	1.5	19	11	1.7[b]	29	14	2.1[b]	82	53	1.5[b]
Lymphatic, hematopoietic system	**111**	**159**	**0.7**[b]	**364**	**313**	**1.2**[b]	**218**	**210**	**1.0**	**298**	**291**	**1.0**	**991**	**973**	**1.0**
Non-Hodgkin's lymphoma	34	43	0.8	105	86	1.2	56	59	1.0	94	84	1.1	289	272	1.1
Hodgkin's disease	11	12	0.9	25	23	1.1	13	15	0.9	21	19	1.1	70	68	1.0
Multiple myeloma	9	30	0.3[b]	34	60	0.6[b]	28	41	0.7[b]	46	58	0.8	117	189	0.6[b]
Leukemias	56	72	0.8	197	141	1.4[b]	117	94	1.3[b]	131	128	1.0	501	434	1.2[b]
Chronic lymphocytic	25	37	0.7[b]	81	70	1.2	52	46	1.1	58	62	0.9	216	215	1.0
Acute nonlymphocytic	24	18	1.3	74	37	2.0[b]	38	26	1.5[b]	41	38	1.1	177	120	1.5[b]

[a] ICD-7 codes = 140–204.

[b] $P < .05$.

ALL CANCER SITES
MALES

TABLE 1D.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	171,749			92,075			35,264			17,170			171,749		
Person-yr in interval	125,334			216,634			123,347			121,051			586,365		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**935**	**1,449**	**0.6**[b]	**2,314**	**2,555**	**0.9**[b]	**1,469**	**1,512**	**1.0**	**1,652**	**1,652**	**1.0**	**6,370**	**7,169**	**0.9**[b]
Buccal cavity, pharynx	**23**	**46**	**0.5**[b]	**85**	**79**	**1.1**	**54**	**45**	**1.2**	**45**	**47**	**1.0**	**207**	**217**	**1.0**
Lip	11	25	0.4[b]	38	43	0.9	25	25	1.0	18	25	0.7	92	117	0.8[b]
Tongue	2	3	0.6	5	6	0.9	9	3	2.7[b]	3	3	0.9	19	16	1.2
Salivary gland	2	4	0.5	4	6	0.6	3	4	0.8	4	4	1.0	13	18	0.7
Gum, other mouth	3	6	0.5	22	11	2.0[b]	5	7	0.8	8	7	1.1	38	32	1.2
Pharynx	5	7	0.7	16	12	1.3	12	7	1.7	12	7	1.6	45	34	1.3
Digestive system	**311**	**554**	**0.6**[b]	**707**	**955**	**0.7**[b]	**462**	**558**	**0.8**[b]	**559**	**591**	**0.9**	**2,039**	**2,657**	**0.8**[b]
Esophagus	14	25	0.6[b]	27	42	0.7[b]	15	24	0.6	30	24	1.3	86	114	0.8[b]
Stomach	88	177	0.5[b]	198	294	0.7[b]	106	168	0.6[b]	136	165	0.8[b]	528	803	0.7[b]
Colon	70	126	0.6[b]	191	223	0.9[b]	140	134	1.0	144	150	1.0	545	633	0.9[b]
Rectum	51	123	0.4[b]	147	212	0.7[b]	89	124	0.7[b]	118	130	0.9	405	589	0.7[b]
Liver, biliary	26	30	0.9	48	54	0.9	40	33	1.2	46	37	1.2	160	154	1.0
Pancreas	49	56	0.9	65	101	0.6[b]	60	61	1.0	70	68	1.0	244	285	0.9[b]
Respiratory system	**155**	**287**	**0.5**[b]	**499**	**515**	**1.0**	**349**	**305**	**1.1**[b]	**387**	**340**	**1.1**[b]	**1,390**	**1,446**	**1.0**
Nasal cavities, sinuses	2	4	0.5	9	7	1.3	2	4	0.5	7	4	1.6	20	19	1.0
Larynx	14	19	0.7	42	34	1.2	21	20	1.0	29	22	1.3	106	97	1.1
Trachea, bronchus, lung	133	250	0.5[b]	435	450	1.0	311	267	1.2[b]	338	299	1.1[b]	1,217	1,266	1.0
Breast	1	3	0.3	3	5	0.6	1	3	0.3	5	4	1.4	10	15	0.7
Prostate gland	126	203	0.6[b]	260	365	0.7[b]	191	222	0.9[b]	214	252	0.8[b]	791	1,042	0.8[b]
Testis	4	5	0.7	18	10	1.8[b]	14	6	2.4[b]	15	6	2.5[b]	51	27	1.9[b]
Kidney, renal pelvis, ureter	78	47	1.7[b]	138	83	1.7[b]	66	50	1.3[b]	66	55	1.2	348	235	1.5[b]
Bladder, other urinary	119	117	1.0	284	211	1.3[b]	161	127	1.3[b]	168	144	1.2	732	598	1.2[b]
Melanoma of the skin	8	12	0.7	29	21	1.4	9	13	0.7	17	14	1.2	63	60	1.1
Eye	2	4	0.5	5	8	0.7	2	4	0.5	0	5	0.0[b]	9	21	0.4[b]
Brain, central nervous system	18	22	0.8	38	40	1.0	24	23	1.0	18	24	0.7	98	109	0.9
Thyroid gland	6	4	1.5	4	7	0.6	4	4	0.9	7	5	1.5	21	20	1.1
Bone	2	3	0.8	2	5	0.4	3	3	1.1	7	3	2.7[b]	14	12	1.1
Connective tissue	2	5	0.4	14	8	1.6	13	5	2.7[b]	6	5	1.2	35	23	1.5[b]
Lymphatic, hematopoietic system	**63**	**93**	**0.7**[b]	**192**	**166**	**1.2**	**92**	**99**	**0.9**	**106**	**109**	**1.0**	**453**	**468**	**1.0**
Non-Hodgkin's lymphoma	18	24	0.8	57	43	1.3[b]	20	25	0.8	32	28	1.1	127	120	1.1
Hodgkin's disease	8	7	1.2	13	11	1.1	5	7	0.7	9	7	1.3	35	32	1.1
Multiple myeloma	6	17	0.3[b]	22	31	0.7	15	19	0.8	13	21	0.6	56	88	0.6[b]
Leukemias	30	45	0.7[b]	97	79	1.2	51	47	1.1	51	52	1.0	229	223	1.0
Chronic lymphocytic	14	25	0.6[b]	47	44	1.1	31	26	1.2	27	29	0.9	119	125	1.0
Acute nonlymphocytic	11	10	1.1	35	19	1.8[b]	12	12	1.0	11	13	0.8	69	54	1.3

[a] ICD-7 codes = 140–204.
[b] $P < .05$.

ALL CANCER SITES
FEMALES

TABLE 1E.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among females in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	<1 yr			1–4 yr			5–9 yr			10+ yr			Total		
No. starting interval	208,192			137,079			67,400			39,260			208,192		
Person-yr in interval	167,319			370,136			256,279			326,638			1,120,371		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**944**	**1,292**	**0.7**[b]	**2,638**	**2,828**	**0.9**[b]	**1,978**	**2,085**	**0.9**[b]	**3,154**	**3,207**	**1.0**	**8,714**	**9,412**	**0.9**[b]
Buccal cavity, pharynx	**14**	**17**	**0.8**	**41**	**37**	**1.1**	**38**	**27**	**1.4**	**55**	**43**	**1.3**	**148**	**124**	**1.2**[b]
Lip	3	3	1.2	10	6	1.8	8	4	2.0	8	7	1.2	29	19	1.5[b]
Tongue	1	3	0.3	5	6	0.8	7	5	1.5	7	7	1.0	20	21	0.9
Salivary gland	5	4	1.3	8	8	1.0	2	6	0.3	13	8	1.7	28	26	1.1
Gum, other mouth	1	5	0.2	8	10	0.8	14	8	1.8	17	14	1.2	40	36	1.1
Pharynx	4	3	1.3	10	7	1.5	7	5	1.4	10	7	1.3	31	22	1.4
Digestive system	**296**	**435**	**0.7**[b]	**849**	**918**	**0.9**[b]	**666**	**676**	**1.0**	**1,129**	**1,083**	**1.0**	**2,940**	**3,111**	**0.9**[b]
Esophagus	6	12	0.5	24	25	1.0	20	18	1.1	33	29	1.1	83	85	1.0
Stomach	68	115	0.6[b]	181	226	0.8[b]	138	158	0.9	197	224	0.9	584	723	0.8[b]
Colon	83	133	0.6[b]	303	290	1.0	266	219	1.2[b]	419	369	1.1[b]	1,071	1,011	1.1
Rectum	43	77	0.6[b]	149	165	0.9	92	121	0.8[b]	220	191	1.2[b]	504	554	0.9[b]
Liver, biliary	33	36	0.9	68	79	0.9	47	61	0.8	84	106	0.8[b]	232	283	0.8[b]
Pancreas	50	42	1.2	77	94	0.8	77	72	1.1	144	126	1.1	348	335	1.0
Respiratory system	**56**	**64**	**0.9**	**226**	**146**	**1.5**[b]	**208**	**112**	**1.9**[b]	**276**	**191**	**1.4**[b]	**766**	**513**	**1.5**[b]
Nasal cavities, sinuses	2	2	1.0	2	4	0.5	2	3	0.6	7	5	1.5	13	14	0.9
Larynx	5	3	1.8	7	6	1.1	8	5	1.7	9	8	1.2	29	21	1.4
Trachea, bronchus, lung	47	54	0.9	207	124	1.7[b]	191	96	2.0[b]	246	165	1.5[b]	691	439	1.6[b]
Breast	129	275	0.5[b]	382	612	0.6[b]	307	450	0.7[b]	466	669	0.7[b]	1,284	2,006	0.6[b]
Female genital tract	**228**	**257**	**0.9**	**556**	**579**	**1.0**	**347**	**420**	**0.8**[b]	**494**	**583**	**0.8**[b]	**1,625**	**1,838**	**0.9**[b]
Cervix uteri	50	91	0.6[b]	145	205	0.7[b]	84	142	0.6[b]	100	169	0.6[b]	379	606	0.6[b]
Corpus uteri	54	71	0.8[b]	148	161	0.9	114	120	0.9	156	180	0.9	472	532	0.9[b]
Uterus, NOS	11	6	1.9	22	11	1.9[b]	11	8	1.4	4	10	0.4[b]	48	35	1.4[b]
Ovary, fallopian tubes	106	75	1.4[b]	210	168	1.2[b]	106	125	0.9	165	184	0.9	587	551	1.1
Kidney, renal pelvis, ureter	59	33	1.8[b]	97	73	1.3[b]	62	55	1.1	109	90	1.2	327	251	1.3[b]
Bladder, other urinary	44	34	1.3	121	76	1.6[b]	88	58	1.5[b]	176	100	1.8[b]	429	269	1.6[b]
Melanoma of the skin	14	18	0.8	49	41	1.2	36	31	1.2	59	47	1.2	158	137	1.2
Eye	5	4	1.4	12	8	1.5	9	6	1.5	13	8	1.5	39	26	1.5[b]
Brain, central nervous system	20	26	0.8	52	58	0.9	31	43	0.7	66	64	1.0	169	191	0.9
Thyroid gland	10	9	1.2	22	19	1.2	16	14	1.1	26	22	1.2	74	64	1.1
Bone	1	2	0.4	5	5	1.0	13	3	3.9[b]	10	5	2.1[b]	29	15	1.9[b]
Connective tissue	5	4	1.1	13	10	1.4	6	7	0.9	23	9	2.5[b]	47	30	1.6[b]
Lymphatic, hematopoietic system	**48**	**66**	**0.7**[b]	**172**	**147**	**1.2**[b]	**126**	**111**	**1.1**	**192**	**182**	**1.1**	**538**	**505**	**1.1**
Non-Hodgkin's lymphoma	16	19	0.8	48	44	1.1	36	33	1.1	62	56	1.1	162	152	1.1
Hodgkin's disease	3	5	0.6	12	11	1.1	8	8	1.0	12	12	1.0	35	36	1.0
Multiple myeloma	3	13	0.2[b]	12	29	0.4[b]	13	22	0.6	33	37	0.9	61	101	0.6[b]
Leukemias	26	28	0.9	100	61	1.6[b]	66	46	1.4[b]	80	75	1.1	272	211	1.3[b]
Chronic lymphocytic	11	12	0.9	34	26	1.3	21	20	1.1	31	33	0.9	97	91	1.1
Acute nonlymphocytic	13	8	1.6	39	18	2.1[b]	26	14	1.8[b]	30	25	1.2	108	66	1.6[b]

[a] ICD-7 codes = 140–204.

[b] $P < .05$.

ALL CANCER SITES
BOTH SEXES
LONG-TERM SURVIVORS

TABLE 1F.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males and females, long-term survivors in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	229,154			56,430			18,121			3,699			379,941		
Person-yr in interval	966,394			338,445			97,336			11,908			1,706,736		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**8,399**	**8,980**	**0.9**[b]	**3,458**	**3,504**	**1.0**	**1,158**	**1,187**	**1.0**	**190**	**168**	**1.1**	**15,084**	**16,580**	**0.9**[b]
Buccal cavity, pharynx	**218**	**188**	**1.2**[b]	**78**	**66**	**1.2**	**19**	**21**	**0.9**	**3**	**3**	**1.0**	**355**	**341**	**1.0**
Lip	81	77	1.1	17	24	0.7	8	7	1.2	1	1	1.1	121	136	0.9
Tongue	26	20	1.3	9	8	1.2	1	3	0.4	0	0	0.0	39	37	1.1
Salivary gland	17	25	0.7	14	9	1.6	3	2	1.2	0	0	0.0	41	44	0.9
Gum, other mouth	49	36	1.4[b]	23	15	1.6[b]	1	6	0.2[b]	1	1	1.0	78	68	1.1
Pharynx	45	31	1.5[b]	15	11	1.4	6	3	1.7	1	1	2.0	76	56	1.4[b]
Digestive system	**2,684**	**3,106**	**0.9**[b]	**1,184**	**1,198**	**1.0**	**415**	**415**	**1.0**	**89**	**61**	**1.5**[b]	**4,979**	**5,768**	**0.9**[b]
Esophagus	86	108	0.8[b]	50	39	1.3	9	13	0.7	4	2	2.3	169	198	0.9[b]
Stomach	623	846	0.7[b]	235	290	0.8[b]	81	88	0.9	17	11	1.5	1,112	1,526	0.7[b]
Small intestine	49	26	1.9[b]	14	10	1.4	4	4	1.0	0	1	0.0	81	49	1.7[b]
Colon	900	866	1.0	400	362	1.1	141	136	1.0	22	21	1.0	1,616	1,645	1.0
Rectum	477	622	0.8[b]	233	233	1.0	86	77	1.1	19	11	1.8[b]	909	1,143	0.8[b]
Liver	73	79	0.9	33	34	1.0	11	13	0.8	4	2	1.9	145	152	1.0
Gallbladder, other biliary	133	148	0.9	50	66	0.8[b]	25	25	1.0	9	4	2.5[b]	252	285	0.9
Pancreas	279	328	0.9[b]	149	136	1.1	52	51	1.0	13	8	1.7	592	620	1.0
Respiratory system	**1,282**	**1,078**	**1.2**[b]	**494**	**386**	**1.3**[b]	**152**	**127**	**1.2**[b]	**17**	**18**	**1.0**	**2,156**	**1,959**	**1.1**[b]
Nasal cavities, sinuses	15	18	0.8	9	7	1.4	5	2	2.4	0	0	0.0	33	33	1.0
Larynx	78	66	1.2	29	22	1.3	8	7	1.2	1	1	1.1	135	118	1.1
Trachea, bronchus, lung	1,144	936	1.2[b]	441	336	1.3[b]	128	112	1.1	15	16	1.0	1,908	1,704	1.1[b]
Other respiratory	5	7	0.7	0	2	0.0	0	1	0.0	0	0	0.0	6	13	0.5
Breast	693	1,071	0.6[b]	362	477	0.8[b]	97	171	0.6[b]	12	24	0.5[b]	1,294	2,021	0.6[b]
Female genital tract	**903**	**998**	**0.9**[b]	**338**	**426**	**0.8**[b]	**136**	**139**	**1.0**	**20**	**18**	**1.1**	**1,625**	**1,838**	**0.9**[b]
Cervix uteri	229	346	0.7[b]	71	130	0.5[b]	23	35	0.6[b]	6	4	1.5	379	606	0.6[b]
Corpus uteri	262	281	0.9	103	129	0.8[b]	47	45	1.1	6	6	1.0	472	532	0.9[b]
Uterus, NOS	33	19	1.7[b]	3	8	0.4	0	3	0.0	1	0	2.9	48	35	1.4[b]
Ovary, fallopian tubes	316	293	1.1	121	132	0.9	40	46	0.9	4	6	0.7	587	551	1.1
Prostate gland	451	588	0.8[b]	170	191	0.9	37	54	0.7[b]	7	8	0.9	791	1,042	0.8[b]
Testis	32	16	2.0[b]	9	5	1.9	6	1	5.0[b]	0	0	0.0	51	27	1.9[b]
Kidney, renal pelvis, ureter	363	261	1.4[b]	128	104	1.2[b]	42	36	1.2	5	5	1.0	675	485	1.4[b]
Bladder, other urinary	654	472	1.4[b]	234	176	1.3[b]	94	60	1.6[b]	16	9	1.8[b]	1,161	867	1.3[b]
Melanoma of the skin	123	106	1.2	52	44	1.2	22	15	1.4	2	2	0.9	221	197	1.1
Eye	28	26	1.1	8	10	0.8	4	3	1.3	1	0	2.9	48	47	1.0
Brain, central nervous system	145	164	0.9	54	65	0.8	27	21	1.3	3	3	1.2	267	300	0.9
Thyroid gland	46	45	1.0	27	19	1.4	5	7	0.7	1	1	1.0	95	84	1.1
Endocrine gland	13	11	1.2	7	4	1.6	3	2	1.9	0	0	0.0	23	21	1.1
Bone	23	15	1.5	13	6	2.4[b]	2	2	1.2	2	0	14.3[b]	43	28	1.6[b]
Connective tissue	46	29	1.6[b]	22	10	2.1[b]	6	3	1.9	1	0	2.2	82	53	1.5[b]
Lymphatic, hematopoietic system	**582**	**523**	**1.1**[b]	**224**	**208**	**1.1**	**70**	**73**	**1.0**	**4**	**10**	**0.4**[b]	**991**	**973**	**1.0**
Non-Hodgkin's lymphoma	161	145	1.1	68	59	1.1	25	21	1.2	1	3	0.3	289	272	1.1
Hodgkin's disease	38	38	1.0	17	14	1.2	4	4	0.9	0	1	0.0	70	68	1.0
Multiple myeloma	62	101	0.6[b]	32	41	0.8	13	15	0.9	1	2	0.5	117	189	0.6[b]
Leukemias	314	234	1.3[b]	103	91	1.1	27	32	0.9	1	5	0.2	501	434	1.2[b]
Chronic lymphocytic	133	116	1.1	46	45	1.0	11	15	0.7	1	2	0.5	216	215	1.0
Acute nonlymphocytic	112	63	1.8[b]	32	27	1.2	9	10	0.9	0	2	0.0	177	120	1.5[b]

[a] ICD-7 codes = 140–204.

[b] $P < .05$.

ALL CANCER SITES
MALES
LONG-TERM SURVIVORS

TABLE 1G.—*Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among males, long-term survivors in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	92,075			17,170			4,529			864			171,749		
Person-yr in interval	339,980			95,066			23,199			2,786			586,365		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**3,783**	**4,067**	**0.9**[b]	**1,275**	**1,258**	**1.0**	**327**	**347**	**0.9**	**50**	**47**	**1.1**	**6,370**	**7,169**	**0.9**[b]
Buccal cavity, pharynx	**139**	**124**	**1.1**	**34**	**36**	**0.9**	**10**	**10**	**1.1**	**1**	**1**	**0.8**	**207**	**217**	**1.0**
Lip	63	67	0.9	14	19	0.7	4	5	0.8	0	1	0.0	92	117	0.8[b]
Tongue	14	9	1.5	3	3	1.2	0	1	0.0	0	0	0.0	19	16	1.2
Salivary gland	7	10	0.7	2	3	0.7	2	1	2.6	0	0	0.0	13	18	0.7
Gum, other mouth	27	18	1.5	7	6	1.3	1	2	0.6	0	0	0.0	38	32	1.2
Pharynx	28	19	1.5	8	6	1.4	3	2	1.9	1	0	4.5	45	34	1.3
Digestive system	**1,169**	**1,513**	**0.8**[b]	**425**	**455**	**0.9**	**112**	**120**	**0.9**	**22**	**16**	**1.4**	**2,039**	**2,657**	**0.8**[b]
Esophagus	42	65	0.6[b]	27	18	1.5	1	5	0.2	2	1	3.5	86	114	0.8[b]
Stomach	304	462	0.7[b]	100	130	0.8[b]	29	31	0.9	7	4	1.9	528	803	0.7[b]
Small intestine	22	13	1.7[b]	4	4	1.0	1	1	0.9	0	0	0.0	36	22	1.6[b]
Colon	331	357	0.9	107	114	0.9	36	32	1.1	1	4	0.2	545	633	0.9[b]
Rectum	236	336	0.7[b]	92	100	0.9	21	26	0.8	5	3	1.5	405	589	0.7[b]
Liver	41	44	0.9	23	15	1.6	5	4	1.1	2	1	3.1	85	79	1.1
Gallbladder, other biliary	48	43	1.1	11	14	0.8	4	4	1.1	2	0	4.5	77	75	1.0
Pancreas	125	161	0.8[b]	54	51	1.1	13	14	0.9	3	2	1.6	244	285	0.9[b]
Respiratory system	**848**	**819**	**1.0**	**303**	**256**	**1.2**[b]	**76**	**74**	**1.0**	**8**	**10**	**0.8**	**1,390**	**1,446**	**1.0**
Nasal cavities, sinuses	11	11	1.0	7	3	2.1	0	1	0.0	0	0	0.0	20	19	1.0
Larynx	63	55	1.2	24	17	1.4	4	5	0.8	1	1	1.5	106	97	1.1
Trachea, bronchus, lung	746	717	1.0	265	225	1.2[b]	66	65	1.0	7	9	0.8	1,217	1,266	1.0
Other respiratory	3	4	0.8	0	1	0.0	0	0	0.0	0	0	0.0	4	7	0.6
Breast	4	9	0.5	3	3	1.1	1	1	1.3	1	0	9.1	10	15	0.7
Prostate gland	451	588	0.8[b]	170	191	0.9	37	54	0.7[b]	7	8	0.9	791	1,042	0.8[b]
Testis	32	16	2.0[b]	9	5	1.9	6	1	5.0[b]	0	0	0.0	51	27	1.9[b]
Kidney, renal pelvis, ureter	204	133	1.5[b]	55	42	1.3	11	12	0.9	0	2	0.0	348	235	1.5[b]
Bladder, other urinary	445	337	1.3[b]	133	108	1.2[b]	31	32	1.0	4	5	0.9	732	598	1.2[b]
Melanoma of the skin	38	34	1.1	11	11	1.0	6	3	1.9	0	0	0.0	63	60	1.1
Eye	7	12	0.6	0	4	0.0	0	1	0.0	0	0	0.0	9	21	0.4[b]
Brain, central nervous system	62	62	1.0	13	18	0.7	5	5	1.0	0	1	0.0	98	109	0.9
Thyroid gland	8	11	0.7	5	4	1.4	2	1	2.2	0	0	0.0	21	20	1.1
Endocrine gland	4	5	0.8	3	2	1.9	1	0	2.3	0	0	0.0	8	9	0.9
Bone	5	7	0.7	4	2	1.9	1	1	2.0	2	0	50.0[b]	14	12	1.1
Connective tissue	27	13	2.0[b]	5	4	1.3	1	1	1.1	0	0	0.0	35	23	1.5[b]
Lymphatic, hematopoietic system	**284**	**266**	**1.1**	**82**	**83**	**1.0**	**21**	**23**	**0.9**	**3**	**3**	**1.0**	**453**	**468**	**1.0**
Non-Hodgkin's lymphoma	77	68	1.1	24	21	1.1	7	6	1.2	1	1	1.3	127	120	1.1
Hodgkin's disease	18	18	1.0	8	5	1.5	1	1	0.7	0	0	0.0	35	32	1.1
Multiple myeloma	37	50	0.7	10	16	0.6	2	4	0.5	1	1	1.9	56	88	0.6[b]
Leukemias	148	127	1.2	40	40	1.0	10	11	0.9	1	1	0.7	229	223	1.0
Chronic lymphocytic	78	71	1.1	23	22	1.0	3	6	0.5	1	1	1.3	119	125	1.0
Acute nonlymphocytic	47	31	1.5[b]	7	10	0.7	4	3	1.4	0	0	0.0	69	54	1.3

[a] ICD-7 codes = 140–204.

[b] $P < .05$.

ALL CANCER SITES
FEMALES
LONG-TERM SURVIVORS

TABLE 1H. *Observed (O) and expected (E) numbers of second primary cancers by years after diagnosis of any first primary cancer among females, long-term survivors in Denmark, 1943–80*[a]

	Yr after first primary cancer diagnosis														
	1–9 yr			10–19 yr			20–29 yr			30+ yr			Total (<1–30+ yr)		
No. starting interval	137,079			39,260			13,592			2,835			208,192		
Person-yr in interval	626,414			243,380			74,137			9,122			1,120,371		
Second primary cancer site	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E	O	E	O/E
All second cancers	**4,616**	**4,913**	**0.9^b**	**2,183**	**2,246**	**1.0**	**831**	**840**	**1.0**	**140**	**121**	**1.2**	**8,714**	**9,412**	**0.9^b**
Buccal cavity, pharynx	**79**	**64**	**1.2**	**44**	**30**	**1.5^b**	**9**	**11**	**0.8**	**2**	**2**	**1.1**	**148**	**124**	**1.2^b**
Lip	18	10	1.9^b	3	4	0.7	4	2	2.2	1	0	3.4	29	19	1.5^b
Tongue	12	11	1.1	6	5	1.2	1	2	0.5	0	0	0.0	20	21	0.9
Salivary gland	10	14	0.7	12	6	2.0^b	1	2	0.6	0	0	0.0	28	26	1.1
Gum, other mouth	22	18	1.2	16	9	1.8^b	0	4	0.0^b	1	1	1.4	40	36	1.1
Pharynx	17	12	1.4	7	5	1.3	3	2	1.6	0	0	0.0	31	22	1.4
Digestive system	**1,515**	**1,593**	**1.0^b**	**759**	**743**	**1.0**	**303**	**295**	**1.0**	**67**	**45**	**1.5^b**	**2,940**	**3,111**	**0.9^b**
Esophagus	44	43	1.0	23	20	1.1	8	8	1.0	2	1	1.7	83	85	1.0
Stomach	319	384	0.8^b	135	160	0.8^b	52	56	0.9	10	8	1.3	584	723	0.8^b
Small intestine	27	14	2.0^b	10	6	1.6	3	3	1.1	0	0	0.0	45	27	1.7^b
Colon	569	509	1.1^b	293	249	1.2^b	105	104	1.0	21	17	1.3	1,071	1,011	1.1
Rectum	241	286	0.8^b	141	133	1.1	65	51	1.3	14	7	1.9^b	504	554	0.9^b
Liver	32	35	0.9	10	19	0.5^b	6	9	0.7	2	1	1.3	60	73	0.8
Gallbladder, other biliary	85	105	0.8^b	39	52	0.7	21	21	1.0	7	3	2.2	175	210	0.8^b
Pancreas	154	167	0.9	95	84	1.1	39	36	1.1	10	6	1.7	348	335	1.0
Respiratory system	**434**	**258**	**1.7^b**	**191**	**130**	**1.5^b**	**76**	**53**	**1.4^b**	**9**	**8**	**1.2**	**766**	**513**	**1.5^b**
Nasal cavities, sinuses	4	7	0.5	2	3	0.6	5	1	4.0^b	0	0	0.0	13	14	0.9
Larynx	15	11	1.4	5	5	0.9	4	2	2.0	0	0	0.0	29	21	1.4
Trachea, bronchus, lung	398	220	1.8^b	176	112	1.6^b	62	46	1.3^b	8	7	1.2	691	439	1.6^b
Other respiratory	2	3	0.6	0	1	0.0	0	0	0.0	0	0	0.0	2	6	0.3
Breast	689	1,062	0.6^b	359	475	0.8^b	96	171	0.6^b	11	24	0.5^b	1,284	2,006	0.6^b
Female genital tract	**903**	**998**	**0.9^b**	**338**	**426**	**0.8^b**	**136**	**139**	**1.0**	**20**	**18**	**1.1**	**1,625**	**1,838**	**0.9^b**
Cervix uteri	229	346	0.7^b	71	130	0.5^b	23	35	0.6^b	6	4	1.5	379	606	0.6^b
Corpus uteri	262	281	0.9	103	129	0.8^b	47	45	1.1	6	6	1.0	472	532	0.9^b
Uterus, NOS	33	19	1.7^b	3	8	0.4	0	3	0.0	1	0	2.9	48	35	1.4^b
Ovary, fallopian tubes	316	293	1.1	121	132	0.9	40	46	0.9	4	6	0.7	587	551	1.1
Kidney, renal pelvis, ureter	159	128	1.2^b	73	62	1.2	31	24	1.3	5	3	1.4	327	251	1.3^b
Bladder, other urinary	209	135	1.6^b	101	67	1.5^b	63	28	2.2^b	12	4	2.8^b	429	269	1.6^b
Melanoma of the skin	85	72	1.2	41	34	1.2	16	12	1.3	2	2	1.2	158	137	1.2
Eye	21	14	1.5	8	6	1.3	4	2	1.9	1	0	4.2	39	26	1.5^b
Brain, central nervous system	83	102	0.8	41	46	0.9	22	16	1.4	3	2	1.5	169	191	0.9
Thyroid gland	38	33	1.1	22	16	1.4	3	6	0.5	1	1	1.1	74	64	1.1
Endocrine gland	9	6	1.5	4	3	1.4	2	1	1.7	0	0	0.0	15	12	1.3
Bone	18	8	2.2^b	9	3	2.6^b	1	1	0.9	0	0	0.0	29	15	1.9^b
Connective tissue	19	16	1.2	17	7	2.6^b	5	2	2.2	1	0	3.0	47	30	1.6^b
Lymphatic, hematopoietic system	**298**	**257**	**1.2^b**	**142**	**125**	**1.1**	**49**	**50**	**1.0**	**1**	**7**	**0.1^b**	**538**	**505**	**1.1**
Non-Hodgkin's lymphoma	84	77	1.1	44	38	1.2	18	15	1.2	0	2	0.0	162	152	1.1
Hodgkin's disease	20	20	1.0	9	9	1.1	3	3	1.0	0	0	0.0	35	36	1.0
Multiple myeloma	25	51	0.5^b	22	26	0.9	11	10	1.1	0	1	0.0	61	101	0.6^b
Leukemias	166	108	1.5^b	63	52	1.2	17	21	0.8	0	3	0.0	272	211	1.3^b
Chronic lymphocytic	55	46	1.2	23	22	1.0	8	9	0.9	0	1	0.0	97	91	1.1
Acute nonlymphocytic	65	33	2.0^b	25	17	1.5	5	7	0.7	0	1	0.0	108	66	1.6^b

[a] ICD-7 codes = 140–204.

[b] $P < .05$.

IV. Appendix

APPENDIX—*Cancer site groups selected for use in this monograph and corresponding ICD codes used by Connecticut and Denmark*

Denmark	Cancer site group	Connecticut
ICD-7 code[a]		ICD-O code[b,c]
140–204[d]	All sites	140–199[d]
140–148	Buccal cavity, pharynx	140–149
140	Lip	140
141	Tongue	141
142	Salivary gland	142
143–144	Gum, other mouth	143–145
145–148	Pharynx	146–148
150–155, 157–159	Digestive system	150–159
150	Esophagus	150
151	Stomach	151
152	Small intestine	152
153	Colon[e]	153, 159.0
154	Rectum, rectosigmoid junction, anus[f]	154
155.0	Liver (primary only)	155
155.1, 155.8	Gallbladder, other biliary	156
157	Pancreas	157
160–162, 164	Respiratory system	160–165
160	Nasal cavities, sinuses	160
161	Larynx	161
162.0, 162.1	Trachea, bronchus, lung	162
164	Pleura, mediastinum, other respiratory[g]	163–165
170	Female breast	174
170	Male breast	175
171–176	Female genital tract	179, 180–184
171	Cervix uteri	180
172	Corpus uteri	182
173–174	Uterus, NOS[h]	179
175	Ovary, fallopian tubes	183
177	Prostate gland	185
178	Testis	186
180	Kidney, renal pelvis, ureter	189.0–189.2
181	Bladder,[i] other urinary	188, 189.3–189.9
190	Melanoma of the skin	173 (M-8720–8780)
192	Eye	190
193	Brain, central nervous system[j]	191–192
194	Thyroid gland	193
195	Endocrine gland	194
196	Bone	170
197	Connective tissue	171

Appendix—*Cancer site groups selected for use in this monograph and corresponding ICD codes used by Connecticut and Denmark* (*continued*)

Denmark	Cancer site group	Connecticut
ICD-7 code[a]		ICD-O code[b,c]
200–204	Lymphatic, hematopoietic system	M-9590–9701, 9730, 9731, 9750, 9800–9940
200, 202	Non-Hodgkin's lymphoma	M-9590–9642, 9690–9701, 9750
201	Hodgkin's disease	M-9650–9662
203	Multiple myeloma	M-9730–9731
204	Leukemias	M-9800–9940
	Acute lymphocytic leukemia[k]	M-9821, 9822
204.0	Chronic lymphocytic leukemia	M-9823
204.2, 204.3	Acute nonlymphocytic leukemia[l]	M-9861, 9862, 9866, 9891–9892, 9801–9802, 9840–9842

[a] Codes are from the World Health Organization: Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, 7th rev. Geneva: WHO, 1957.

[b] Codes are from the World Health Organization: International Classification of Diseases for Oncology, 1st ed. Geneva: WHO, 1976.

[c] ICD-O topography code is given unless morphology (M) is indicated.

[d] Both registries exclude nonmelanoma skin cancers from the "all sites" category.

[e] Denmark includes rectosigmoid junction with the colon.

[f] Denmark excludes anus and rectosigmoid junction from the rectum.

[g] Connecticut excludes thymus, 164.0, from the other respiratory sites; Denmark includes mediastinum only in code 164.

[h] Denmark excludes uterus, not otherwise specified (NOS) from the corpus uteri, as a first primary site; Connecticut combines these 2 sites as a first primary.

[i] Denmark includes papillomas with invasive bladder cancers.

[j] Denmark includes benign tumors of the brain and central nervous system in code 193.

[k] Denmark does not present separate tabulations for acute lymphocytic leukemia.

[l] Danish Cancer Registry adapted ICD-7 codes to categorize separately acute nonlymphocytic leukemias. These codes include erythroleukemia and acute myeloid leukemia and exclude lymphocytic leukemias.

CONTRIBUTORS

William J. Blot, Ph.D.
Biostatistics Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

John D. Boice, Jr., Sc.D.
Radiation Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Louise A. Brinton, Ph.D.
Environmental Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Bendix Carstensen
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Rochelle E. Curtis
Radiation Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Susan S. Devesa, Ph.D.
Biostatistics Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Marianne Ewertz, M.D.
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

John T. Flannery
Connecticut Tumor Registry
Department of Health Services
Hartford, Connecticut 06106

Joseph F. Fraumeni, Jr., M.D.
Epidemiology and Biostatistics Program
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Mark H. Greene, M.D.
Environmental Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Elizabeth B. Harvey, Ph.D.
Radiation Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Shelia K. Hoar, Sc.D.
Environmental Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Daniel A. Hoffman, Ph.D.
Radiation Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Robert N. Hoover, M.D.
Environmental Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Hjalgrim S. Jensen
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Ole M. Jensen, M.D.
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Arlene F. Kantor, Dr.P.H.
Environmental Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Ruth A. Kleinerman
Radiation Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Jens B. Knudsen, M.D.
Department of Surgery
Finsen Institute
Strandboulevarden 49
DK-2100 Copenhagen, Denmark

Frederick P. Li, M.D.
Clinical Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Joan V. Liebermann, M.D.
Radiation Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Elsebeth Lynge
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Joseph K. McLaughlin, Ph.D.
Biostatistics Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Henning T. Mouridsen, M.D.
Department of Oncology I
Finsen Institute
Strandboulevarden 49
DK-2100 Copenhagen, Denmark

Jørgen Olsen, M.D.
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Anne Østerlind, M.D.
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Anne Prener, M.D.
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Mikael Rørth, M.D.
Department of Oncology II
Finsen Institute
Strandboulevarden 49
DK-2100 Copenhagen, Denmark

Geert Schou
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Bent L. Sørensen, M.D.
Department of Surgery
Finsen Institute
Strandboulevarden 49
DK-2100 Copenhagen, Denmark

Hans H. Storm, M.D.
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
DK-2100 Copenhagen, Denmark

Margaret A. Tucker, M.D.
Environmental Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Jerome Wilson, Ph.D.
Radiation Epidemiology Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

Deborah M. Winn, Ph.D.
Biostatistics Branch
Division of Cancer Etiology
National Cancer Institute
Bethesda, Maryland 20892

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